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EDITORIAL

REVIEW ARTICLE

ORIGINAL ARTICLES

CASE REPORTS

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KUWAIT MEDICAL JOURNAL (KMJ)
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INTRODUCTION

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Book

Roberts NK. The cardiac conducting system and His bundle electrogram. New York, Appleton-Century-Crofts, 1981; 49-56.

Book chapter

Philips SJ, Whisnam JP. Hypertension and stroke, In: Laragh JH, Bremner BM, editors. Hypertension: pathophysiology, diagnosis, and management. 2nd Ed. New York: Raven Press; 1995. p 465-478.

Weblinks

U.S. positions on selected issues at the third negotiating session of the Framework Convention on Tobacco Control. Washington, D.C.: Committee on Government Reform, 2002. (Accessed June 4, 2003, at http://www.house.gov/reform/min/inves.tobacco/index_accord.htm.)

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Editorial

Can Science Teach a Thing or Two to Nature?

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The Journal of the Science of Healing Outcomes, State College, Pennsylvania, USA and Mangalore, India*
Manipal University, Manipal India**
The Middlesex Medical School, University of London, UK#
Northern Colorado University, USA##

Kuwait Medical Journal 2012; 44 (2): 90 - 91

"A great man is always willing to be little"
Ralph Waldo Emerson

Science is a method only and its job is to try and understand nature. With the advent of paper money, human greed, which follows money like a shadow, became more important in science than all the other principles governing scientific research. It was shocking to read the following study in a leading American Journal some time ago. The inference of the study makes a mockery of nature's best kept secret - mother's milk is the best tonic for the immune system of the new born; the longer one can take mother's milk the healthier that person will live. Once we stop taking mother's milk, we lose our enzymes to digest any milk for the rest of our lives! Mother's milk contains the best fatty acid for the development and good health of the immune system - sodium mono-laureate. Along with mother's milk, the child is also hard wired to pick up dirt from room floorings while crawling to stimulate its immune system to develop antibodies against most germs - nature's method of vaccination.

Now comes this study from the CDC, a conventionally authentic organization, looking after the health of the public! The fault is not with science but with the man behind the science. Even in the past there have been instances of those writing papers from such organizations being hired by vested interests! This is nothing new and I am sure it is another one of those attempts by such elements in the lucrative vaccine industry. Let us see the inference of the study.

"The lower immunogenicity and efficacy of rotavirus vaccines in poor developing countries could be explained, in part, by higher titers of IgA and neutralizing activity in breast milk consumed by their infants at the time of immunization that could effectively reduce the potency of the vaccine. Strategies to overcome this negative effect, such as delaying breast-feeding at the time of immunization, should be evaluated"[1].

Ethen Huff, a staff reporter of Natural News writes: "The CDC researchers began their investigation by searching for answers as to why children from underdeveloped countries typically do not respond as well to the live oral rotavirus vaccine as children in developed countries typically do. They came to the conclusion that breast milk, which is packed with immune-building immunoglobulin A (IgA), lactoferrin, lysozyme, and various other important immune factors, inhibits the vaccine from working.

Breast milk, of course, is a young child's lifeline. It naturally builds immunity during childhood development, and provides perfect and balanced nutrition necessary for human growth. Withholding breast milk in order to accommodate the rotavirus vaccine, as the CDC researchers suggest, is an absolutely insane notion that will deprive children of vital nutrition and proper immune development.

But it is ludicrous that notions like these are birthed from philosophies that view drugs and vaccines as being equal, or even superior, to natural food. Oral rotavirus vaccines contain live viruses, they have questionable efficacy to begin with, and they are even known to cause rotavirus infections. They are also linked to causing a variety of negative side effects, including diarrhea, which is a condition the vaccine is supposed to prevent!"[2].

There is so much controversy in the whole science of vaccination. It will not be a good idea to promote the idea of asking mothers not to breast feed their babies around vaccinations of which today there are 26 in all in the USA. In essence, if the mother is breast feeding for only a few months this policy will deny the child the best elixir nature intended to keep the child's immune system going all its life. I have been very strongly feeling that the essential need for science

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as a method is to understand nature and NEVER to oppose nature and teach nature a thing or two! When it happens in the vaccine arena this makes it all the more dangerous. Although I am not a vaccine nihilist, I feel many of the vaccines that we give do not do what we think they ought to do.

This is slowly coming into light despite the enormous efforts on the part of the vaccine lobby to stop such truth from emerging. Recent controversy of Autism and MMR vaccination is an example. It is now revealed that even editors and investigators of prestigious medical journals had received hefty amounts to build a case to tarnish the image of that poor researcher, Dr. Wakefield to get his name erased from the General Medical Council's (GMC) list after succeeding in getting The Lancet to retract his original paper. Dr. Wakefield has enough data to file a defamation suit against the concerned people as also against the GMC. I think he has already filed the case. The Guardian reported his case: In a statement, the BMJ said: "The BMJ is on notice that Andrew Wakefield has issued defamation proceedings, not in London as might be ordinarily expected as concerns a predominately English publication, but in Texas, USA, where he now lives." A recent case of a child dropping down dead soon after a new 'Flu shot created lots of controversy in the USA with opposing groups trying to highlight this and the other group trying to bury the hatchet[3].

When I read the following news item I was not just shocked but felt sorry for our profession as a whole. "PrisonPlanet.com reports that Oxford's Susanne Sheehy and Joel Meyer, together authored the paper, entitled 'Should Participation in Vaccine Clinical Trials be Mandated?'[4]. In it, the duo recommends "Compulsory involvement in vaccine studies" in response to a general lack of willing volunteers, many of whom are not exactly comfortable sacrificing their bodies and their health to have a toxic brew of untested chemicals injected into them." I do not blame the volunteers. Stories abound as to how such volunteers are recruited in poorer countries where human life is just a statistic! The following two reports will reveal more details. "It was revealed back in 2008 that at least 14 Argentinean children died as part of an experimental vaccine trial conducted by a British pharmaceutical giant[5]. Also in 2008, 21 homeless individuals in Poland died during an avian flu vaccine experiment. Prisoners of War have been other easy targets in the past[6].

I only pray and hope that science confines itself to its pristine duty of trying to understand nature and assist nature's methods, if we could. Let us fight this menace collectively as suggested by Ryunosuke Satroo: "Individually we are just one drop. Together we are an ocean." How true? David Wootton in his classic Bad Medicine: Doctors Harming since Hippocrates has done a serious study of the happenings over the decades and centuries in modern medicine[7]. In fact, this book makes Bernard Shaw's Doctors Dilemma look like a child's play. It made me feel bad about my cherished profession.

"A foolish consistency is the hobgoblin of little minds, adored by little statesmen and philosophers and divines. With consistency a great soul has simply nothing to do."

Ralph Waldo Emerson

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Review Article

Proximal Tibial Osteotomy in Medial Compartment Osteoarthritis: How High is High?

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ABSTRACT

Proximal tibial osteotomy (PTO), which can be performed using various techniques, is a common procedure for the treatment of medial compartment osteoarthritis of the knee. Changes in the biomechanics of knee may cause problems in the long term, depending on the technique that was performed. Whichever technique is used, the level at which the osteotomy is performed is a significant factor in any changes in biomechanics and for potential problems in future surgery. The relationship between the techniques applied and the names used throughout its progression is investigated in this review, which briefly evaluates the historical improvement of PTO applied in the treatment of knee osteoarthritis. Denomination defined by the first practitioners of different osteotomies that were used in the treatment of knee osteoarthritis and identified under different names were investigated in the literature. Compatibilty of technique defined by using the word "high" and different techniques were evaluated. The contribution of alteration in surgical techniques on nomenclature has lead to standard usage with time. The term "high", which has been used for longer than four decades, does not cover all of these techniques. Nomenclature of osteotomies performed for the treatment of medial compartment osteoarthritis would therefore be more appropriate, if it were used in such a way as to define the actual level of osteotomy. We believe that osteotomies performed distal to the tibial tubercle must be defined as 'upper tibial' or 'proximial tibial' instead of 'high', or related osteotomy level and method must be clearly stated in each individual case.

KEY WORDS: arthroplasty, osteoarthritis, osteotomy, patella, tibia

INTRODUCTION

Osteotomy is one of the oldest approaches in orthopedic surgery for correcting lower limb deformity[1]. Today, the most widely used technique is high tibial osteotomy (HTO), which is performed with the aim of reducing deformity caused by the occurrence of medial compartment osteoarthritis (MCOA) of the knee, one of the most frequently seen indications for corrective osteotomy[2]. The aim of HTO in MCOA of a varus knee is decompression of the degenerated medial compartment, in order to delay the progress of cartilage degeneration[3,4]. HTO is a highly effective procedure for relieving pain, correcting deformity and improving function in cases of MCOA of the knee, and can be performed using a variety of techniques that are associated with varying clinical results[4-11].

Several different osteotomy techniques have been described for MCOA with varus deformity[11-22]. Over the past decade there has been an explosion of interest in developing modifications of surgical techniques, new surgical instrumentation, and new fixation devices, as well as increasing interest in the use of external fixation devices, and computed tomography-free navigation systems which aim to improve the accuracy, reliability, and safety of realignment osteotomy[23]. The three principal techniques to produce valgus realignment of the proximal tibial articular surface are lateral closing wedge osteotomy (Fig. 1 a - c), medial opening wedge osteotomy (Fig. 2 a - c), and dome osteotomy (Fig. 3). A dome osteotomy can be performed with convexity on the superior or inferior surface of the osteotomy level. The level of osteotomy must be agreed on as well as the appropriate technique. Osteotomies above, below, and behind the tubercle have all been previously described[13,15,19]. The pros and cons of osteotomies performed proximal or distal to the tibial tuberosity and of closing-opening wedge versus dome osteotomy should be considered.

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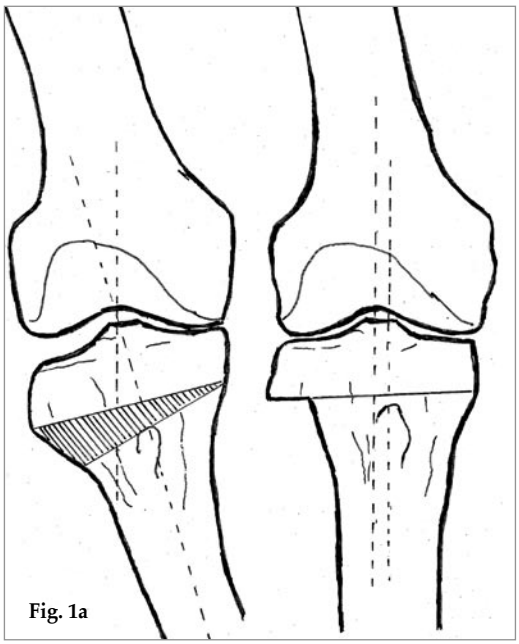
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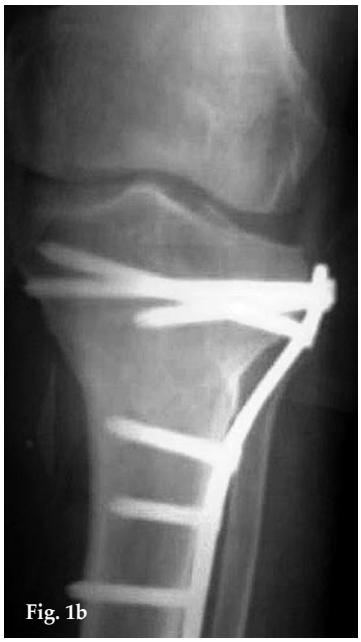
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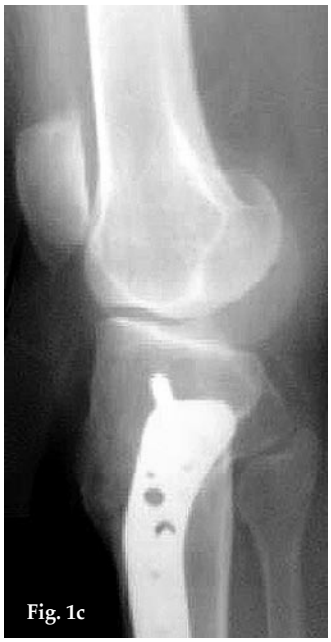


Fig. 1c

Fig. 1a. Lateral closing-wedge high tibial osteotomy. (**b)** Anteroposterior radiograph of a 56-year-old female patient in the 5th post-operative year. (**c)** Lateral radiograph of the same patient.

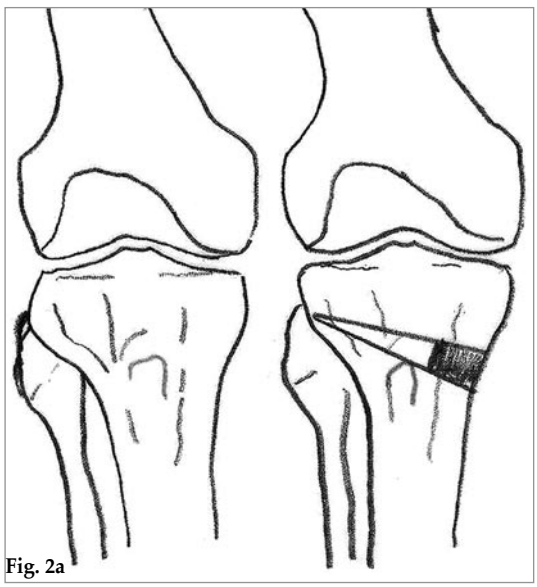
Performing a HTO with the correct technique on a suitable patient is the basis for a successful result. The selection of the type of osteotomy should take into consideration the patient, the disease and joint characteristics. For the treatment of MCOA there should be an "a la carte" approach, with each case being considered according to the state of the deformity[2].

In this article, the relationship between the nomenclature and the different techniques of proximal tibial osteotomy with varying biomechanics is discussed.

HISTORY

History of osteotomy of the knee

Osteotomy of the proximal tibia has been used for more than a century to correct angular deformity in the setting of rickets, poliomyelitis, and post-traumatic situations[24]. The first known report on osteotomy performed on the tibia was written in 1851 by Joseph Anton von Mayer[25]. Mayer named the operation "resection tibiae cuneiformis" and between the years 1839 - 1854 he performed 20 osteotomies on rickets-induced deformities[26,27]. Wardle stated that osteotomy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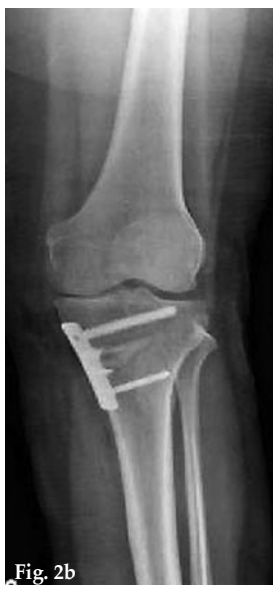
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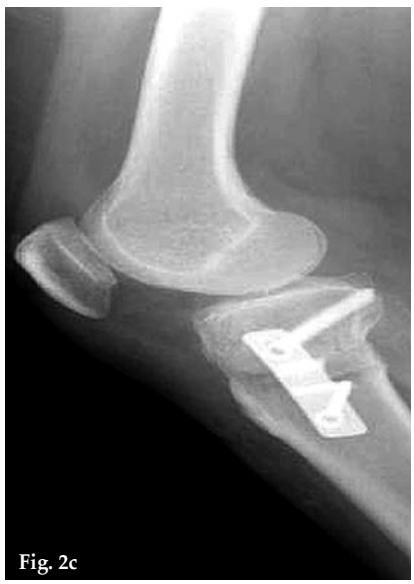


Fig. 2c

Fig. 2 a: Medial opening wedge high tibial osteotomy. (**b)** Anteroposterior radiograph of 51-year-old female patient in the 2nd post-operative year. (**c)** Lateral radiograph of the same patient.

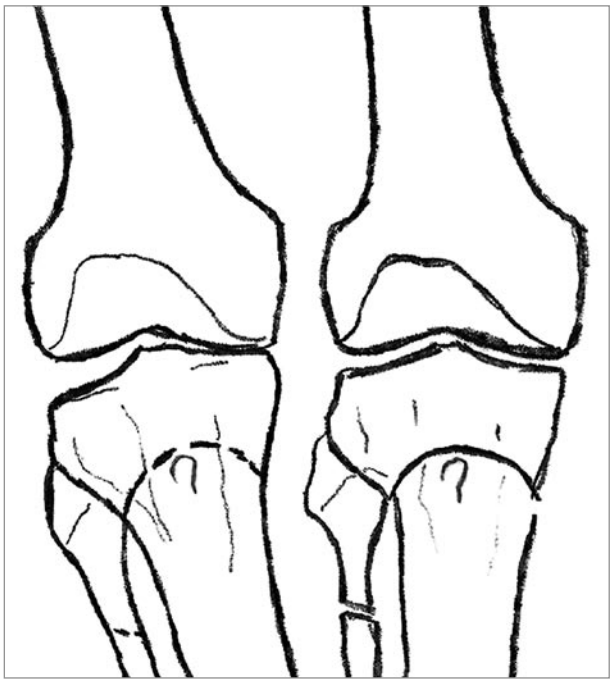


Fig. 3: "Barrel vault" dome tibial osteotomy performed proximal to the tibial tuberosity

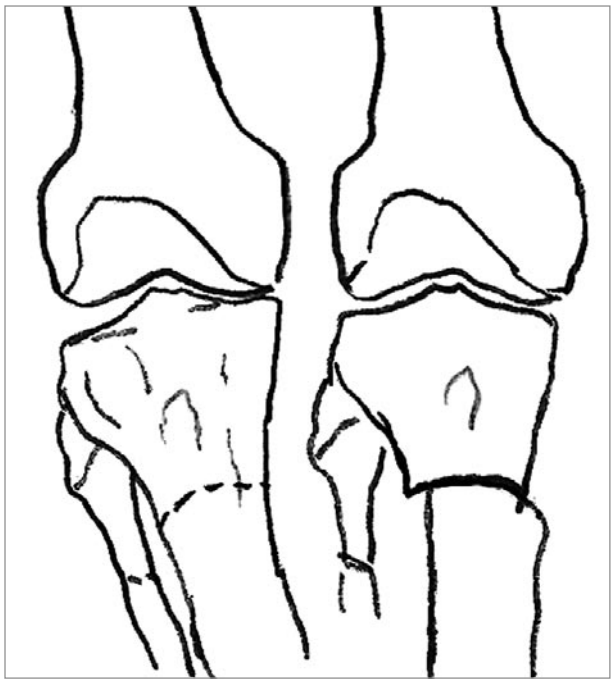


Fig. 4: "Ball and socket" dome tibial osteotomy performed distal to the tibial tuberosity

of the tibia combined with division of the fibula had been done in Liverpool since 1928[28]. The surgeons who practised it at that time usually had to deal with deformity of the knee in adults, as a consequence of childhood rickets.

The standard textbooks of the first half of the 20th century did not discuss realignment. Arthur Steindler, Paul Collanna, and Willis Campbell did not even refer to tibial osteotomy for treatment of painful osteoarthritis of the knee[29]. Osteotomy for treatment of osteoarthritis of the knee in modern English literature was first reported by Jackson in 1958 at the Joint Meeting of the Orthopedic Associations[12]. In 1961, Jackson and Waugh were the first to publish their results on the treatment of osteoarthritis of the knee with a tibial osteotomy[13]. They reported that they were inspired by the success of an intertrochanteric osteotomy for relieving pain in the osteoarthritic hip. The operation had been performed both in Liverpool and other centers, and there were published results relating to its use in the treatment of the osteoarthritic knee joint[13]. Jackson and Waugh described "ball-and-socket" dome tibial osteotomy performed distal to the tibial tuberosity for osteoarthritis (Fig. 4). In 1961, Smillie[14] reviewed his experience of linear osteotomy of the tibial table for the correction of genu recurvatum, genu varum and genu valgum deformities of epiphysial origin. He performed the osteotomy about one centimetre below the articular surface and concluded that there were possible applications for his operation in selected cases of osteoarthritis. In 1962, Wardle[15] published his results of a tibial osteotomy done transverse and about four inches distal to the tibial tubercle. In 1964, Gariepy[16] described high tibial valgus osteotomy, a closing wedge technique performed proximal to the tibial tubercle that was further modified and popularized by Coventry in his classic paper published in 1965[17]. This technique has not been modified since it was first reported by Gariepy in 1960[30]. Various other forms of closing wedge osteotomy have also been described[20,21]. Wagner[20] in 1977, described an oblique metaphyseal proximal tibial osteotomy just below the tibial tubercle.

A medial opening wedge osteotomy proximal to the tibial tubercule was first applied in 1951 by Debeyre *et al*[31] for MCOA. In 1987 Hernigou *et al*[19] published a 10 - 13 year follow-up of 93 patients operated on with this technique. Puddu *et al*[32] and Lobenhoffer and Agneskirchner[3] described a modified opening wedge osteotomy in 2000. Turi *et al*[33] developed the technique of progressive opening wedge osteotomy by hemicallotasis in 1987, and this method was subsequently modified by other authors[5,6,34,35]. This osteotomy can be performed above the tibial tubercle or at its distal part.

The dome or curviplane high tibial osteotomy was introduced by Blaimont[31] in 1969 and popularized by Maquet[18] in 1976. He described a "barrel vault osteotomy" similar to the "ball-and-socket" osteotomy of Jackson. However, this osteotomy is proximal to the tibial tubercle. It is semicylindrical, and its concavity is downward, circumscribing the tibial tuberosity. Paley and Tetsworth[36], in a detailed analysis of advances in the diagnosis and treatment of lower limb deformities

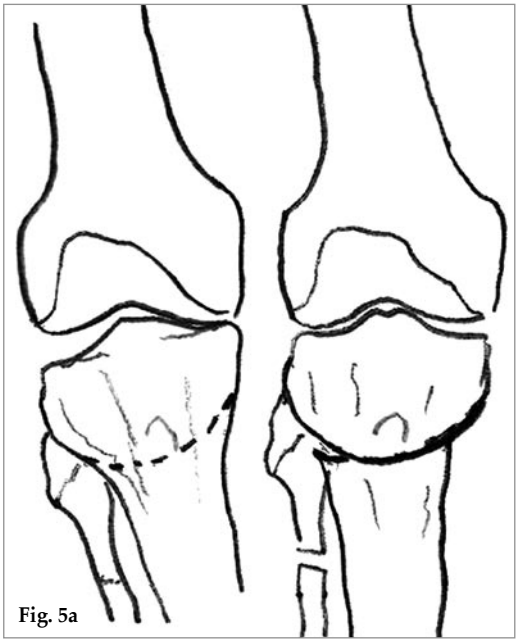


Fig. 5a

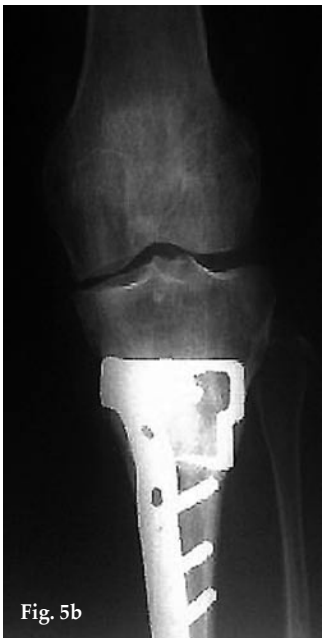


Fig. 5b

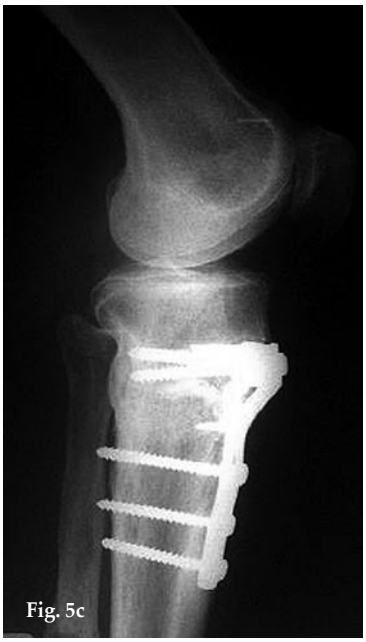


Fig. 5c

Fig. 5 a: Focal dome high tibial osteotomy. (**b)** Anteroposterior radiograph of 62-year-old female patient in the 7th post-operative year. (**c)** Lateral radiographs of the same patient.

reported a new approach for HTO in the treatment of MCOA in 1994[22]. This procedure was named "focal dome osteotomy" because, when seen from above, it has the shape of a reverse dome distal to the tibial tuberosity (Fig. 5 a - c).

History of nomenclature of proximal tibial osteotomy techniques

Various techniques of HTO, performed as treatment for MCOA of the knee, have different nomenclature. A few of them are, "proximal tibial osteotomy", "upper tibial osteotomy", "valgus tibial osteotomy", "tibial osteotomy" "osteotomies around the knee", "dome osteotomy", "closing or open wedge high tibial osteotomy" and "focal dome osteotomy". Osteotomy for treatment of osteoarthritis of the knee was first reported in 1958, and Jackson performed osteotomies distal to the tibial tubercule and named this approach as "osteotomy through the upper tibia....."[12]. In 1961, Jackson and Waugh[12] were the first to publish an article about tibial osteotomies entitled "Tibial Osteotomy for Osteoarthritis of the Knee" in which they performed dome tibial osteotomy at the level of / or distal to the tibial tuberosity. In their next article on this subject, published in 1963, the osteotomy level was still below the tibial tubercle and the article was entitled "Tibial Osteotomy for Osteoarthritis of the Knee"[37]. In 1961 Smillie[14] performed the osteotomy about one centimeter below the articular surface and the technique was named "upper tibial osteotomy". In 1962, Wardle[15] published an article entitled "Osteotomy of the Tibia and Fibula" in which osteotomy was performed transversely distal to the tibial tubercle. In the same year, Venemans[38] performed an osteotomy immediately distal to the tibial tubercle and he reported it as "Tibial osteotomy for osteoarthritis of the knee". Gariepy was the first to use the term "High Tibial Osteotomy" in 1964[16]. This osteotomy, which was performed proximal to the tibial tubercle was reported in his article "Genu varum treated by high tibial osteotomy". He stated that the advantages of doing a wedge osteotomy at a high level, *i.e.*, above the insertion of the patellar tendon, are obvious both for mechanical reasons and for bone healing[30]. Coventry modified and popularized the technique described by Gariepy and reported it in his 1965 article "Osteotomy of the upper portion of the Tibia for Degenerative Arthritis of the Knee"[17]. Devas[39] in 1969 and Harris and Kostuik[40] in 1970 performed the osteotomy again above the tibial tubercle and used the term "high tibial osteotomy". However in 1966, Gunn[41] reported his cases as "high" tibial osteotomy, but in his article osteotomies were performed at the level of the tibial tubercle or lower. In fact, as Jackson and Waugh moved the level of osteotomy from inferior of the tibial tubercle to superior, they also changed the title of their article "Tibial Osteotomy for Osteoarthritis of the Knee" to "High Tibial osteotomy for Osteoarthritis of the Knee"[13,37,42]. In 1969, Bauer *et al*[43] preferred "high rather than shaft osteotomy of the tibia" and they termed osteotomies performed superior to the insertion of the patellar tendon as high.

HTO, as defined by Gariepy[16] and popularized by Coventry[17] is a procedure where the osteotomy is performed proximal to the attachment of the patellar tendon. In the following years, as the use of external

fixators became more widespread, an increase was seen in the performance of various modifications of HTO (below the tibial tubercle). Following the detailed works of Paley and Tetsworth[36] on lower extremity deformities, new approaches to high tibial osteotomy were developed[22]. In 1964, the term 'high' was first used by Gariepy[16] to define an osteotomy performed proximally to the tibial tubercle and it gained widespread use as this method became more popular. In contrast to this, Gunn[41] was the first one to use this term to define the osteotomies performed distal to the tibial tubercle, and it is still used for an increasing number of osteotomies in this anatomical region[5-9,21]. For example, the title of the article which was published in 2011 and evaluates the clinical and the radiological results of the medial open wedge osteotomy applications is stressed as "High tibial open wedge osteotomy below the tibial tubercle"[44].

Bony anatomy of the proximal tibia

The tibia, the larger and medial bone of the lower leg, has a large upper end and a smaller lower end. The expanded proximal end is a bearing surface for body weight that is transmitted through the femur. It has massive medial and lateral condyles, an intercondylar area and a tibial tuberosity. The upper end is widely expanded, and there is a prominent tuberosity projecting anteriorly from its lower part. The tuberosity shows a smooth oval prominence set obliquely; it receives the quadriceps insertion *via* the patellar ligament. A line across the tibial tuberosity marks the distal limit of the proximal tibial growth plate[45,46].

Long bones are simply divided into three anatomical regions: proximal, diaphysis and distal or epiphysis, metaphysis and diaphysis. A certain distinction can only be made by histological examination.

DISCUSSION

Possible Long Term Consequences of Changes in Biomechanics Following Osteotomy

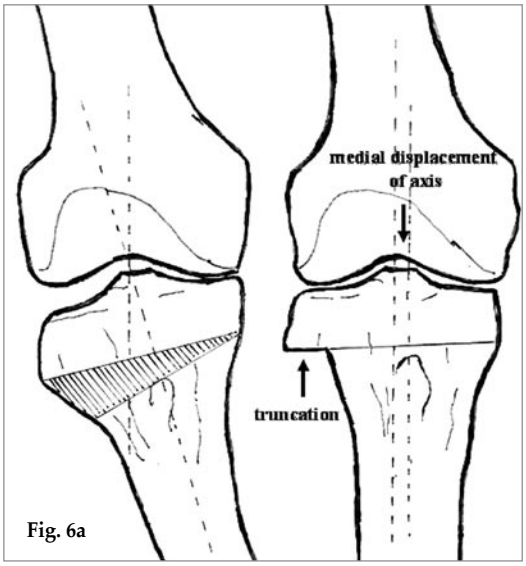
Deformity of the knee associated with osteoarthritis (OA) is a common presenting complaint to the orthopedic surgeon. A mal-alignment of the lower limb as a result of unicompartmental OA of the knee can accentuate stress on the damaged articular cartilage, which in turn leads to progression of OA. The rationale behind HTO is to correct the angular deformity of the knee thereby reducing the load transfer across the arthritic medial compartment[4,47]. High tibial osteotomy is an attractive option in many of these cases because it preserves the knee joint and delays the need for total knee arthroplasty (TKA). Survivorship analysis has shown that the reliable longevity of a HTO is approximately six years[48]. In their 2004 meta-analysis, Virolainen and Aro[49] reported that HTO had an average probability of good or excellent results in 75.3% of the patients after 60 months and 60.3% after 100 months.

In the 1960s, with limited treatment options for arthritis, osteotomy was indicated for all types of arthritic joint conditions[13,17]. As medium and long-term results of osteotomy began to appear in the literature along with the development of total knee arthroplasty, the indications and contra-indications for osteotomy have gradually been defined. The generally accepted criteria for suitable patients for HTO are men below the age of 60 and pre-menopausal women, who have a high level of daily activity, or those with occupation related diseases, non-inflammatory MCOA, and stability of the joint without subluxation, at least 90° flexion and less than 15° flexion deformity[2]. However, it is not clearly defined if there is a relationship between these criteria and the desired method of osteotomy. Paley *et al*[22] recommended that these should not be taken as absolutes: in the treatment of MCOA there should be an 'à la carte' approach, with each case being considered according to the state of the deformity. The most appropriate method of osteotomy will depend on the requirements of each patient[11,50]. Gaasbeek *et al*[11] recommended that where a large degree of correction is required, the preference should be for a distal tuberosity osteotomy. Brinkman *et al*[50] used this type of osteotomy in patients with a pre-existing low patella, and considered it in opening-wedge corrections > 8 to 10º.

Many patients with medial compartment osteoarthritis of the knee ultimately require a TKA. Although many cases of osteotomy have no need for TKA in the medium or long-term, every case of MCOA is a potential candidate for TKA. The published conversion rate of an osteotomy to a TKA is between 20 and 50% at 10 years[49-53]. Therefore HTO should not increase the difficulty of any future procedures that may be undertaken; primary TKA carried out following HTO has been shown to be more difficult and less successful than where HTO has not been carried out.

Although the most important factor for a successful HTO is not the level of osteotomy, nor the type of fixation, but rather the ability to obtain the precise amount of correction to place the mechanical axis in the lateral compartment, the technique used and the level at which the osteotomy is performed may be important factors when the necessity for TKA arises in the future[54]. Depending on the osteotomy technique, outcomes such as patella infera, lateral truncation, reduced tibia bone stock, alterations in the joint line and medial displacement of the tibial axis, which can arise for various reasons, play a role in the reduced success of any subsequent TKA (Fig. 6 a, b).

There is still some controversy around the merits or otherwise of closing wedge, open wedge and dome



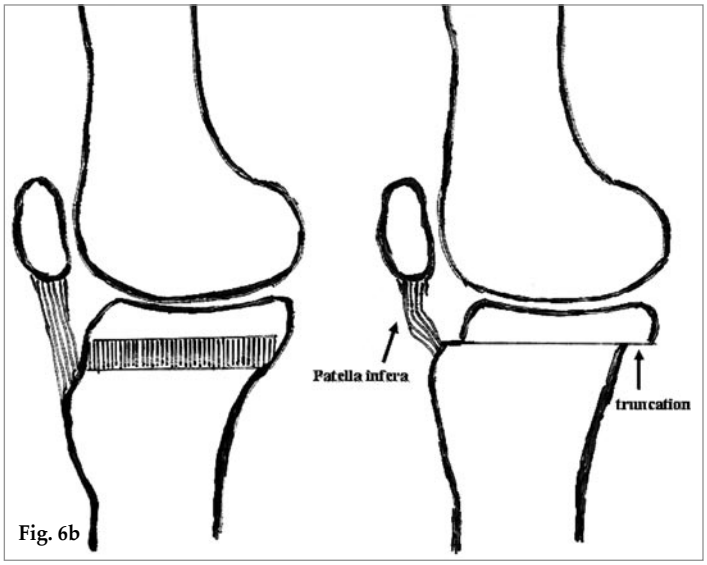


Fig. 6: Anatomical changes following osteotomy of the proximal tibia
a: Medial displacement of axis and truncation after lateral closing wedge osteotomy
b: Patella infera due to contracted patellar tendon

osteotomies and for which cases the osteotomy should be performed proximal or distal to the tibial tuberosity. The majority of cases with all three of these techniques are usually performed proximal to the tibial tubercle to gain the advantage of early bone union. The disadvantages of these osteotomies are primarily the potential negative ramifications for future TKA. Wedge resection of the cancellous bone in the proximal tibia will result in truncation, particularly where there has been a large deformity correction, and will also remove important structural bone support which may be required for any subsequent TKA[22]. As the osteotomy axis is not the same as the deformity axis, a medial translation deformity will result. Following a closing wedge resection the patellar tendon insertion on the tibial tuberosity moves closer to the joint line, which generally results in patella infera secondary to scarring in the retropatellar fat pad and the restraining retinacular structures around the patella[11,22].

The decision to use one over the other must be based on the surgeon's philosophy and clinical experience[23]. However, HTO with medial opening wedge has gained in popularity over recent years as a viable alternative to traditional lateral closed wedge osteotomy for the surgical management of MCOA[44,55-57]. This approach allows earlier rehabilitation, does not require a fibular osteotomy, reduces the frequency of neurovascular complications, and is easier to convert to a TKA compared to the traditional closed-wedge alternative[56,58]. However, opening-wedge HTO can result in complications such as patella baja and delayed union at the osteotomy site due to the bony gap created[59].

In open wedge osteotomy, the most reliable fixation and augmentation techniques are still controversial. Many methods have been used to fill the osseous gap and these include; bone grafts (autograft or allograft), synthetic bone substitutes with or without platelet-rich plasma, growth factors and bone marrow stromal cells. Gold standards seem to be locked plates and autologous bone graft[60]. Bone graft is generally considered to be the most successful bone filling material because of its osteoconductive, osteoinductive and osteogenic properties. Nevertheless, autograft harvesting involves increased operative time and the donor site morbidity, while allograft has lower osteoinductive properties and carries disease transmission risk. The bone substitutes attempt to reduce these risks, but there are still some concerns about their resistane to compressive loads and biological degradability. The use of bone cement is not recommended in order to achieve a more biological repair of the osteotomy site[61]. Encouraging results have been reported with the use of platelet-rich plasma, bone marrow stromal cell and growth factors, associated both with bone grafting and with bone substitute augmentation[60,62,63].

Only, a few studies have compared the results after opening-wedge and closing-wedge osteotomy[64-66]. The current evidence-base suggests that there is no difference in clinical outcome or incidence of complications. Opening-wedge HTO increases the risk of a greater posterior slope angle, patella baja and a reduced hip-knee angle compared to closing-wedge HTO during the early post-operative period. Furthermore, longer-term, well controlled RCT's are now required to develop the evidence-base. Accordingly, future study should include an assessment of cost-effectiveness by evaluating duration of hospital stay, rehabilitation and time until return to occupational or sporting pursuits[53].

In many subjects with poor results of TKA following previous HTO, patella infera, which causes a drastic change in patella-femoral biomechanics, has been reported[67,68]. In a study by Scuderi *et al*[69] patella infera was seen in 89% cases following HTO. Patella infera can be explained in many ways. Shortening of the distance between the tibial tuberosity and the joint line during osteotomies proximal to the tibial tubercle, distalization of the tuberosity and scarring of the patellar ligament resulting in shortening are among these possible reasons of patella infera. Because of these reasons, various modifications of these osteotomy techniques (closing-open wedge, dome) have been described. The studies of Jacobs and Murphy[21] on closing wedge osteotomies, Gaasbeek *et al*[11] on open wedge osteotomies and Paley *et al*[22] on dome osteotomies may be given as examples. In all these three techniques osteotomies are performed distal to the tibial tubercle with the aim of reducing the occurrence of patella infera.

Although, during the last decade these techniques have gained popularity, to the best of our knowledge no clinical results have yet been published of their effects on subsequent TKA. In literature, there are only a few studies focusing on the effects of different types of previous osteotomies on the subsequent TKA[53,54]. These studies were performed on a limited number of subjects and the methods compared are only closing wedge or dome osteotomies, both of which were performed proximal to the tibial tubercle. There is no study covering the results of TKA performed on subjects with previous osteotomy levels distal to the tibial tubercle, as well as open wedge osteotomies which are performed proximal to the tibial tubercle. However, in their 2008 study on cadavers, Whitehead *et al*[70] stated that TKA is potentially harder following closed wedge osteotomies compared to open wedge.

CONCLUSION

The fact that patients undergoing osteotomy are candidates for future TKA and that different osteotomies with similar clinical results have different impacts on future TKA, necessitates a more detailed analysis of osteotomy location. The term 'high', which has been widely used since 1964 for various osteotomy levels, may be misleading when it covers all of the proximal tibial osteotomies performed. We believe that, instead of 'high', osteotomies performed distal to the tibial tubercle must be defined as 'upper tibial' or 'proximial tibial', or that osteotomy level and method must be clearly stated in each individual case.

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Original Article

Nosocomial Bacteria on Doctors' Mobile Phones

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ABSTRACT

Objectives: 1) To determine the rate and type of colonization of a random sample of doctors' mobile phones with nosocomial bacteria in Al-Adan Hospital, 2) Frequency of the practice of using of mobile phones by the doctors while on duty, and 3) To recommend mobile phone disinfection measures based on the study
Design: Prospective cross-sectional study
Setting: Al-Adan Hospital, Kuwait
Subjects: Eighty-two doctors from different departments and different positions (seniors and juniors)
Interventions: Microbiological study of doctors' mobile phones
Main Outcome Measures: Rate and type of colonization of the mobile phones with pathogenic and /or nosocomial organisms
Results: Out of 82 mobile phones, 40 (48.78%) were positive for bacterial colonization. While 42 (79.25%) isolates were coagulase negative staphylococci, only five (9.43%) were coagulase positive (*S. aureus*). Out of the 42 coagulase negative staphylococci 18 (42.86%) were *S. epidermidis.*
Conclusion: Doctors mobile phones may be colonized with pathogenic bacteria. Controlled studies are required to assess the disinfection methods of mobile phones in hospitals.

KEY WORDS: bacteria, colonization, mobile phones

INTRODUCTION

Hospital Acquired Infections (HAI) occur at a rate of 5 - 10 per 100 hospital admissions. Since 1861, Semmelweis showed that bacteria are transmitted to the patients by the contaminated hands of health care workers. Furthermore, many objects in the clinical environment are known to be contaminated with pathogenic bacteria. These objects are considered to be a potential reservoir for such bacteria, with the subsequent risk of cross-infection and HAI. Doctors' white coats, stethoscopes, otoscopes and electronic thermometers have been investigated as potential vectors of nosocomial infection[1-3]. In the recent years, there has been a widespread use of mobile phones by health care workers inspite of restriction due to initial concern regarding electro-magnetic interference (EMI). The annual meeting of the American Society of Anaesthesiologists 2003 concluded that the small risk of EMI between cell phones and medical devices is outweighed by the potential benefits of improved communication, which could eventually help reduce the risk of medical errors[3-5]. Mobile phones are considered as vital equipment in medical care and are extensively used for communication in clinical settings.

Many studies around the globe have documented the colonization of health care workers' mobile phones with pathogenic bacteria. The majority of these studies report an overall colonization rate of 9 - 25% with bacteria known to cause HAI such as MRSA, Pseudomonas spp, and Acinetobacter spp. There are reports for both the level and type of bacterial colonization of mobile phones of the health care workers. These reports raised concerns of potential cross-infection especially in highly sensitive areas such as operating rooms and intensive care units. The colonization of doctors hands with pathogenic bacteria after the use of fixed and mobile phones even following hand disinfection is also documented. The studies also investigated the relationship between the type of bacterial colonization of both the doctors' hands and their mobile phones. Some studies also suggested that there is a geographical element in relation to prevalence[6-11]. However, no such investigation has been done in Kuwait. The aim of this study was to investigate the colonization of a random sample of doctors' mobile phones with bacteria, during their working hours in a major medical institution in Kuwait. We were aiming to investigate the rate and type of bacterial colonization of the mobile phones, looking for pathogenic and / or nosocomial organisms.

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MATERIAL AND METHODS

A prospective, cross-sectional analysis was conducted in a 600–bedded teaching hospital. The investigation was approved by the Ministry of Health Ethics Committee and written informed consent was obtained from the study participants. A total of 82 doctors' mobile phones were tested during a two months-period from June 16th, 2009 to August 10th, 2009. The phones were swabbed in the middle of the working day. The doctors were chosen randomly while working in the wards, clinics, emergency department, intensive care unit and operating rooms. The mobile phones were tested with a wet sterile swab smeared on the key pads, back and the sides of the phones. The swabs were transferred to the microbiology laboratory within one hour of collection.

The inoculations were made on sheep blood agar plates which were incubated at 37 ºC overnight. The bacterial isolates were subjected to preliminary observations like colony characteristics, catalase, oxidase, coagulase test and Gram staining. The final identification for majority of the isolates was carried out in MicroScan 96 automated system (Dade Behring, West Sacramento, CA, USA) using Positive Combo 21 panels. However, *Streptococcus viridans* was identified by conventional tests including resistance to optochin.

A data collection sheet was filled by each participant. It included information about gender, speciality, usage of mobile phones, frequency and method of cleaning of the mobile phones and time and place of collection of the sample.

RESULTS

Out of the eighty-two doctors who participated in the study forty-eight (59%) stated that they use their mobile phones most of the time compared to the use of the hospital fixed phones. Sixty-seven (82%) of them used the mobile phones for patient related issues. Fifty (61%) of them stated that they do not clean the mobile phone at all.

A total of 53 bacterial isolates were recovered from 40 mobile phones of the doctors. We did not isolate any Gram negative bacterial species in our study. The number of different bacterial species isolated is shown in Table 1.

While 42 (79.25%) isolates were coagulase negative staphylococci, only five (9.43%) were coagulase positive (*S. aureus*). All the five *S.aureus* strains were sensitive to the usual antibiotics (except one strain showing resistance to erythromycin) including oxacillin as per MicroScan report using Positive Combo 21 panels. No *S.aureus* strain was found to be MRSA or MDRO. Out of the 42 coagulase negative staphylococci 18 (42.86%) were *S. epidermidis*. Whereas, majority of the mobile phones were colonized with only one bacterial species, twelve showed growth of two or three species / strains.

Two *S. aureus* strains were isolated from the mobile phones of two surgeons (one of them was working in the OR at the time of collection). The remaining three isolates of *S.aureus* were from a pediatrician, a physician while working in the wards and from a nephrologist while doing his rounds in the ICU. The two isolates of *Streptococcus viridans* were from a physician and from an obstetrician while working in the ward.

DISCUSSION

Mobile phones are part of the commonly used patients care items and can serve as vectors for pathogenic organisms. The use of mobile phones has increased in the clinical setting and occurs in close proximity to patients[1-5]. In a study from Australia, mobile phones photo messaging was used for 27 cases of hand trauma for correspondence between the registrar and the consultant in the emergency department[12]. Our study also showed that majority of doctors used their mobile phones more often than the fixed phones and the use was mostly for patient-related issues.

The results of our study are in conformity with the results of previous studies regarding the contamination of doctors' mobile phones with pathogenic bacteria[5-11]. Similar to what was reported before, coagulase negative staphylococci were the most commonly isolated species which are known to produce nosocomial infections, especially, in immunocompromised patients and in certain wards like adults and neonatal intensive care units.

We could not demonstrate any Gram negative bacilli and enterococci in our study. This is similar to what was documented in a previous study[1]. This finding may be due to the fact that these organisms usually need a moist environment for survival which is not present on the surface of the mobile phones.

Table 1: Number of bacterial species isolated from doctors' mobile phones

S. aureus	Coagulase Negative Staphylococci		*Streptococcus viridans*	*Micrococcus* and related Spp,	Total isolates
	S. epidermidis	* Other Spp.			
5	18	24	2	4	53

* *S. hominis* 12, *S. capitis* 3, *S. haemolyticus* 3, *S. auricularis* 3, *S. warneri* 1, *S. xylosus* 1, *S. cohnii* 1

In contrast to other studies, we could not demonstrate the presence of certain other nosocomial organisms such as MRSA, Pseudomonas and Acinetobacter spp. Despite a wide variability in the level and type of bacteria discovered depending on the clinical setting and the country of origin of the study, the majority of the studies reported an overall rate of 9 - 25% contamination with bacterial species known to cause HAI. Some studies reported a rate of 8% contamination with MRSA, 6.6% for Acinetobacter, and 3% for Pseudomonas[6].

The tested mobile phones were personal phones, *i.e.*, they are used by the doctors inside and outside hospital setting. The potential of mobile phone to spread the infection in the community is an important argument in any debate regarding benefits and risks of mobile phone use by health care workers. A complete ban of mobile phones in hospital is unrealistic and cannot be consistently enforced. On the other hand, till now there are no standard recommendations for cleaning mobile phones by health care workers as compared to the standard guidelines for hand washing. Although mobile phones are often decontaminated using alcohol, well-controlled studies in this context are limited. Further studies are needed to show possible methods of decontamination of mobile phones in order to implement active preventive strategies that meet hospital guidelines for infection control.

There are two limitations of our study. First, the small sample size; we would have demonstrated more organisms if we increased the size of the study population. Second, our study was restricted to doctors' mobile phones. A larger study is needed on the mobile phones used by other health care workers such as nurses, physiotherapists and radiology technicians to have a wider assessment on different bacterial species colonization.

In view of the results of our study, we suggest that staff education regarding good hygienic practice, strict infection control precautions, regular cleaning and decontamination of mobile phones and not using mobile phones close to patients remain important measures to reduce the transmission of pathogenic bacteria in the hospital through mobile phones.

CONCLUSION

Doctors' mobile phones may be colonized with pathogenic organisms. There is a potential for these phones to spread the infection inside and outside hospital settings. Well-controlled studies are needed on standardization of mobile phone decontamination, as restriction on their use is not a practical solution.

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Original Article

Is Medical Education Really Stressful? A Prospective Study in Selcuk University, Turkey

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ABSTRACT

Objective: To explore, if medical education is really a risk factor for medical students' well-being due to their various type of exposures and the resultant psychological morbidity, reported
Design: A prospective questionnaire based study
Setting: Selcuk University Meram Medical Faculty, Konya, Turkey
Subjects: New entrants to the medical faculty
Intervention: A self-administered questionnaire consisting of Hospital Anxiety and Depression Scale (HADS) with demographic variables and questions related to visions about medical career was administered prospectively. The important life events, challenges confronted and suicidal ideas were evaluated.
Main Outcome Measure: Anxiety and depression levels
Results: During three years, 138 (84.1%), 98 (62.8%) and 101 (64.7%) students answered the questionnaire and the mean anxiety scores were 7.35 ± 3.17, 8.47 ± 4.26 and 7.36 ± 4.14, respectively ($p = 0.05$). The mean depression score of 5.03 ± 3.37 in the first year increased to 6.66 ± 4.11 in the second year and decreased to 5.62 ± 3.62 in the third year ($p = 0.00$). Male students had higher depression than females in all three assessments ($p < 0.05$). In Y3, students who did not make informed decisions were feeling more anxiety ($p = 0.00$). Students who had suicidal idea had higher scores in HADS ($p < 0.05$).
Conclusion: Medical education uniquely did not seem to be a stressful process for medical students. Out of school problems seem to be worsening their psychology more than the school problems they faced as negative events and as the reasons of their suicidal idea.

KEY WORDS: anxiety, depression, medical education, stress, student

INTRODUCTION

We want to begin with the words of an author "Getting things right for patients means first getting things as good as we can for those who will deliver their care"[1]. A healthy workforce and healthy medical students should be beneficial to the quality of teaching and learning and the quality of doctors ultimately produced[2]. Medical education is the first step of these health care professionals which is defined as a long, traumatic and stressful journey[2,3-11]. Medical schools were also defined as the greatest source of stress the medical students had ever experienced[6,7,12]. Stress, health concerns and emotional problems increase during medical education[10]. Of course there are personal and professional factors that influence student's well-being, but student satisfaction with the learning environment is suggested to be a critical factor which was associated with student burn-out[4,5,13,14]. Besides the noted positive effect of considerable degree of stress which provides an impetus to learn and achieve[2,15] there is an important negative impact on cognitive functioning and learning by decreasing the psychological well-being[2,3,16]. Although medical students perceived their health to be good, a significant and consistent increase of stress symptoms was found during the entire medical program[10]. The information about medical students stress and personal and professional factors influencing these stresses may lead to interventions to design a more student-friendly curricula and may trigger their counseling and rehabili tation[4,5,10,16,17]. Medical schools need to equip graduates with the skills necessary to assess personal distress, determine its effect on their care of patients, recognize when they need assistance, and develop strategies to promote their own well-being[5,16].

There is an increasing interest for more attention to the high levels of stress commonly perceived among medical students[2,7,14,18,19]. Contrary to the importance,

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the magnitude and periodicity of the distress of medical students is still unclear and only a small number of prospective studies have been done[10,19]. Prospective studies to determine the sources of medical students' stress and the association of psychological morbidity with demographic variables are needed[14,17]. Therefore, this three-year prospective study was designed to achieve the following aims: (1) to define the incidence of anxiety and depression among new entrant medical students prior to full effect of medical education (2) to describe the probable factors contributing to their anxiety and depression (3) to analyze the changes in anxiety and depression levels during their three-year medical training.

SUBJECTS AND METHODS

Medical education in Selcuk University Meram Faculty of Medicine is divided into preclinical (1st, 2nd and 3rd years), clinical (4th and 5th years), and internship (6th year) periods. The selected participants of this prospective study were 164 new entrant medical students in 2007. These students were evaluated after a four-month period in 2008 (A1) and results of that study with the comparison of second year students were published in another journal[14]. For this study, students were re-evaluated in one year periods in 2009 (A2) and in 2010 (A3) *via* a redesigned questionnaire. This paper presents the data of the first (A1), second (A2) and third (A3) assessments. In summary, medical students' anxiety and depression levels were followed from the first year to the end of preclinical years between 2008 and 2010. This survey was carried out by avoiding the stressful times of exams and transition problems of new academic year beginning. Every student was briefed about the aim of the study and verbal consent was taken. The students were also assured about anonymity and confidentiality of their responses given in the questionnaire. The questionnaires were distributed during a lecture and completed questionnaires were collected at the end of the same lecture. The local ethics committee approved the study.

Questionnaire form

Data was obtained through a questionnaire consisting of three parts:

1. Questions concerning socio-demographic data; gender, hometown, family income *etc*
2. A. Questions concerning education-related details; reasons for selecting a career in medicine, expectations from medical career, being pleased with the career selection, idea of abandon *etc*.
   B. Questions about recent life events; experience of an important problem in the past six months, suicidal idea, if any, and the time and reasons of the suicidal idea and predilections

Table 1: The main characteristics of students who participated in the study

Characteristics	2007-2008		2008-2009		2009-2010		p-value
	N	(%)	N	(%)	N	(%)	
Gender							0.67
Man	70	50.4	45	45.9	45	44.6	
Woman	69	49.6	53	54.1	56	55.4	
Hometown							0.39
Rural	18	12.9	13	13.3	8	7.9	
Urban	121	87.1	85	86.7	93	92.1	
Family income							0.00
0-1000 TL	65	46.8	34	34.7	26	25.7	
1001 TL and over	74	53.2	64	65.3	75	74.3	
Information about medical education							0.16
Yes	82	59.0	63	64.3	72	71.3	
No	57	41.0	35	35.7	29	28.7	
Information about working conditions							0.14
Yes	72	51.8	61	62.2	64	63.4	
No	67	48.2	37	37.8	37	36.6	
The reasons for medical career							0.34
Occupation guarantee	59	42.2	55	56.1	55	54.5	
External influences	15	10.8	9	9.2	10	9.9	
Individual reasons	61	43.9	31	31.6	32	31.7	
Other factors	4	2.9	3	3.1	4	4.0	
Expectations from medical career							0.00
Esteem/prestige	99	71.2	52	53.1	63	62.4	
Better economic conditions	16	11.5	20	20.4	13	12.9	
Occupational satisfaction	24	17.3	20	20.4	18	17.8	
Other	0	0.0	6	6.1	7	6.9	
Total	139	100.0	98	100.0	101	100.0	

Table 2: Anxiety levels of students according to different variables in three year

Variables	Mean Anxiety Scores					
	2007 - 2008	p*	2008 - 2009	p*	2009 - 2010	p**
Gender		0.67		0.90		0.32
Man	7.48 ± 3.13		8.53 ± 4.42		7.82 ± 4.45	
Woman	7.26 ± 3.22		8.43 ± 4.16		7.00 ± 3.88	
Hometown		0.46		0.00		0.78
Rural	7.88 ± 3.51		11.38 ± 3.42		7.75 ± 4.71	
Urban	7.29 ± 3.12		8.03 ± 4.22		7.33 ± 4.12	
Family income		0.00		0.59		0.49
0-1000 TL	8.13 ± 2.97		8.79 ± 4.26		7.84 ± 4.27	
1001 TL and over	6.70 ± 3.19		8.31 ± 4.28		7.20 ± 4.11	
Information about medical education		0.77		0.11		0.00
Yes	7.43 ± 3.17		7.96 ± 4.02		6.68 ± 3.77	
No	7.28 ± 3.19		9.40 ± 4.57		9.06 ± 4.58	
Information about working conditions		0.28		0.00		0.00
Yes	7.09 ± 3.18		7.54 ± 3.77		6.35 ± 3.53	
No	7.67 ± 3.14		10.02 ± 4.61		9.10 ± 4.57	
The reasons for medical career		0.23		0.29		0.70
Occupation guarantee	7.40 ± 3.17		9.20 ± 4.36		7.70 ± 4.28	
External influences	7.86 ± 3.27		7.88 ± 3.05		6.10 ± 4.72	
Individual reasons	7.42 ± 3.15		7.41 ± 4.38		7.25 ± 3.63	
Other factors	4.25 ± 1.89		8.00 ± 2.64		6.75 ± 5.56	
Expectations from medical career		0.13		0.62		0.79
Esteem/prestige	7.25 ± 2.98		8.90 ± 4.12		7.12 ± 4.12	
Better economic conditions						
Occupational satisfaction	8.81 ± 3.95		8.45 ± 4.96		7.15 ± 3.86	
Others	6.91 ± 3.21		7.40 ± 3.74		7.94 ± 3.76	
			8.50 ± 5.08		8.42 ± 6.10	
Groupwise mean scores	7.35 ± 3.17		8.47 ± 4.26		7.36 ± 4.14	0.05

p* p-value according to one-way ANOVA test

P** p-value according to student-t test

Table 3: Depression levels of students according to different variables in three year

Variables	Mean Depression Scores					
	2007 - 2008	p*	2008 - 2009	p*	2009 - 2010	p**
Gender		0.02		0.00		0.00
Man	5.65 ± 3.64		7.95 ± 4.29		6.68 ± 3.93	
Woman	4.40 ± 2.93		5.56 ± 3.66		4.76 ± 3.12	
Hometown		0.03		0.01		0.92
Rural	6.55 ± 3.34		9.23 ± 5.01		5.50 ± 3.58	
Urban	4.80 ± 3.31		6.27 ± 3.84		5.63 ± 3.64	
Family income		0.00		0.01		0.76
0-1000 TL	6.12 ± 3.43		8.00 ± 4.43		5.80± 3.95	
1001 TL and over	4.08 ± 3.00		5.95 ± 3.78		5.56 ± 3.52	
Information about medical education		0.26		0.15		0.09
Yes	4.76 ± 2.88		6.22 ± 3.79		5.23 ± 3.64	
No	5.42 ± 3.94		7.45 ± 4.60		6.58 ± 3.43	
Information about working conditions		0.00		0.02		0.09
Yes	4.31 ± 3.06		5.95 ± 3.87		5.17 ± 3.80	
No	5.80 ± 3.51		7.83 ± 4.28		6.40 ± 3.17	
The reasons for medical career		0.44		0.03		0.38
Occupation guarantee	5.10 ± 3.72		7.27 ± 4.41		6.07 ± 3.94	
External influences	6.26 ± 3.65		8.77 ± 4.81		4.40 ± 3.50	
Individual reasons	4.68 ± 2.91		5.03 ± 2.71		5.09 ± 2.97	
Other factors	4.75 ± 2.98		6.00 ±4.58		6.75 ± 3.94	
Expectations from medical career		0.00		0.62		0.37
Esteem/prestige	4.53 ± 2.81		6.40 ± 4.18		5.22 ± 3.84	
Better economic conditions	8.62 ± 4.81		7.75 ± 4.52		5.92 ± 3.30	
Occupational satisfaction	4.70 ± 2.94		6.40 ± 3.81		6.05 ± 2.77	
Others			6.16 ± 3.31		7.57 ± 3.86	
Groupwise mean scores	5.03 ± 3.36		6.66 ± 4.11		5.62 ± 3.62	0.00

p* = p-value according to one-way ANOVA test

P** = p-value according to student-t test

Table 4: The mean anxiety and depression scores of students in A2 related to education-related questions and recent life events

Quiestions	2008-2009 (A2)					
	N	%	Mean Scores	Anxiety p	Mean Scores	Depression
Any important problem in the past 6 months?				0.00		0.00
Yes	45	45.9	10.15 ± 4.26		8.28 ± 4.07	
No	53	54.1	7.05 ± 3.74		5.28 ± 3.66	
If yes; what was the problem?				0.95		0.47
Don't want to say	17	37.8	10.29 ± 4.19		8.64 ± 4.10	
Personal problems	6	13.3	10.50 ± 4.23		10.16 ± 2.78	
Problems about intimates	6	13.3	10.66 ± 4.13		6.50 ± 3.72	
Problems about school	15	35.6	9.68 ± 4.74		7.87 ± 4.51	
Any suicide idea?				0.03		0.02
Yes	6	6.1	12.66 ± 4.58		10.66 ± 6.15	
No	88	89.8	8.14 ± 4.12		6.28 ± 3.81	
Sometimes	4	4.1	9.50 ± 4.35		9.00 ± 4.54	
If yes; The time of the suicidal idea				0.44		0.75
Don't want to say	2	20.0	11.00 ± 1.41		8.50 ± 2.12	
Last one year	3	30.0	8.66 ± 4.93		8.66 ± 5.50	
More than one year before	5	50.0	13.20 ± 4.91		11.40 ± 6.58	
If yes; The reason of suicidal idea				0.96		0.61
Don't want to say	3	30.0	11.33 ± 5.13		7.33 ± 3.51	
Own problems	4	40.0	11.00 ± 6.16		11.75 ± 7.63	
School problems	3	30.0	12.00 ± 3.00		10.33 ± 3.51	
Pleased with the career selection?				0.12		0.00
Always	26	26.5	7.26 ± 3.00		4.15 ± 3.56	
Generally	40	40.8	8.15 ± 4.80		6.82 ± 3.73	
Sometimes	25	25.5	9.92 ± 4.25		8.24 ± 3.33	
Never	7	7.1	9.71 ± 4.11		9.42 ± 6.29	
Any idea of abandon?				0.00		0.10
Yes	19	19.4	11.63 ± 4.01		8.15 ± 4.66	
No	56	57.1	7.67 ± 4.00		5.94 ± 3.64	
Sometimes	23	23.5	7.82 ± 4.01		7.17 ± 4.50	
If yes or sometimes; Reason for abandon				0.39		0.81
Don't want to say	9	20.5	9.22 ± 2.90		7.33 ± 2.64	
Individual factors	22	50.0	10.45 ± 4.23		8.22 ± 5.15	
External factors	1	2.3	12.00 ± 0.00		8.00 ± 0.00	
Institutional factors	12	27.3	7.91 ± 5.17		6.66 ± 4.43	
Predilection				0.09		0.00
Again medical career	70	71.4	8.38 ± 4.49		5.71 ± 3.57	
Never medical career	7	7.1	11.71 ± 4.68		10.85 ± 6.06	
Double minded	21	21.4	7.71 ± 2.77		8.42 ± 3.81	

3. Hospital Anxiety and Depression Scale (HADS); a self reported scale for anxiety and depression levels of medical students[20]

Hospital Anxiety and Depression Scale (HADS)

This scale consists of 14 items, seven for anxiety and seven for depression. Each item was rated on a scale from 0 to 3[20]. It was found to perform well in assessing anxiety disorders and depression in both somatic, psychiatric situations and primary care patients and general population[21]. Validity and reliability of the Turkish version of the scale had been made and the cut-off levels were determined as seven for depression and 10 for anxiety in Turks[22]. Psychological status of students was assessed *via* the cut-off levels according to scale separately for anxiety and depression. But it should be known that the HADS is a screening measure and can only be used to estimate a likely prevalence of anxiety and depression and cannot be used to establish a firm diagnosis.

Statistical analyses

All analyses were performed with SPSS 13.0 software. Descriptive statistics were given in terms of counts and percentages, respectively. We used frequency tables to calculate the prevalence rates of demographic variables. Student's t-test and one-way ANOVA for parametric variables and chi-square and Kruskal–Wallis for non-parametric variables were established. All tests were two tailed and the significance level used was a p value < 0.05.

RESULTS

Data in this study were obtained from 164 new entrant medical students in a three year follow up. Out of the 164 new registered students, 139 (84.7%) participated in the first assessment (A1, in 2008)[14]. One year later in the second assessment (A2) eight failed students were eliminated and 98 students (62.8%) were evaluated. In the third assessment (A3) 101 students (64.7%) fulfilled the questionnaire.

Table 5: The mean anxiety and depression of students in A3 related to education-related questions and recent life events

Quiestions	2009-2010 (A3)					
	N	%	Mean Scores	Anxiety p	Mean Scores	Depression
Any important problem in the past 6 months?				0.00		0.02
Yes	44	43.6	8.77 ± 4.04		6.52 ± 3.13	
No	57	56.4	6.28 ± 3.92		4.92 ± 3.83	
If yes; what was the problem?				0.46		0.98
Don't want to say	23	52.3	8.60 ± 3.98		6.69 ± 3.36	
Personal problems	9	20.5	10.11 ± 3.25		6.22 ± 2.72	
Problems about intimates	3	6.8	10.33 ± 5.50		6.33 ± 2.30	
Problems about school	9	20.5	7.33 ± 4.55		6.44 ± 3.57	0.00
Any suicide idea?				0.00		
Yes	9	8.9	11.77 ± 3.83		10.00±3.24	
No	81	80.2	6.30 ± 3.49		4.86±3.31	
Sometimes	11	10.9	11.54 ± 4.10		7.63±2.94	
If yes; The time of the suicidal idea				0.86		0.35
Don't want to say	5	25.0	10.80 ± 2.77		7.00 ± 1.22	
Last one year	13	65.0	11.92 ± 4.40		9.07 ± 3.70	
More than one year before	2	10.0	12.00 ± 4.24		10.50 ± 2.12	
If yes; The reason of suicidal idea				0.84		0.65
Don't want to say	5	25.0	12.00 ± 3.08		9.00 ± 3.39	
Own problems	7	35.0	12.14 ± 4.63		9.42 ± 3.15	
School problems	8	40.0	11.00 ± 4.03		7.87 ± 3.44	
Pleased with the career selection?				0.00		0.00
Always	23	22.8	4.91 ± 3.27		3.52 ± 2.96	
Generally	51	50.5	7.52 ± 3.71		5.56 ± 3.36	
Sometimes	20	19.8	7.80 ± 4.06		6.50 ± 3.57	
Never	7	6.9	13.00 ± 4.35		10.42 ± 2.25	
Any idea of abandon?				0.00		0.00
Yes	26	25.7	9.38 ± 4.57		6.69 ± 3.50	
No	46	45.5	5.76 ± 3.39		4.76 ± 3.87	
Sometimes	29	28.7	8.10 ± 3.94		6.03 ± 3.05	
If yes or sometimes; Reason for abandon				0.51		0.27
Don't want to say	14	25.5	7.62 ± 3.54		6.78 ± 2.80	
Individual factors	28	50.9	9.50 ± 4.59		6.75 ± 3.50	
External factors	6	10.9	8.83 ± 4.70		6.00 ± 3.89	
Institutional factors	7	12.7	7.57 ± 4.03		4.14 ± 1.95	
Predilection				0.03		0.00
Again medical career	76	75.2	6.89 ± 3.92		4.97 ± 3.42	
Never medical career	9	8.9	10.55 ± 6.16		8.77 ± 3.59	
Double minded	16	15.8	7.81 ± 3.14		6.93 ± 3.45	

Aproximately fifty percent of the participants were female in A1 (49.6%, n = 69). The female ratio was 54.1% and 55.4% in the prospective years. There were no significant differences between the students participating at the three assesments (A1 – A3) in terms of socio-demographic variables except family income. In all three assessments "occupation guarantee" was the main reason of a medical career decision. Table 1 summarizes the socio-demographic variables and education related characteristics of the students.

The mean anxiety score of the students' of A1 was 7.35 ± 3.17. Students whose family incomes were above 1000 Turkish Lira (TL) had higher anxiety scores ($p < 0.05$). In A2, students from rural parts of Turkey and those who had no information about working conditions before decision making were more anxious ($p = 0.00$). In A3 students who did not make informed decisions were feeling more anxiety ($p = 0.00$). The mean anxiety and depression scores of students' in three years are shown in Table 2.

As regards depression the mean depression score was the highest in A2 and was found to be 6.66 ± 4.11 ($p = 0.00$). Male students had significantly higher scores in depression scale in all three assessments ($p < 0.05$). In A1 and A2 "coming from rural areas" and "lower family incomes" were the main factors which were making students more depressed ($p < 0.05$). The depression scores of students' for three years are represented in Table 3.

The mean anxiety and depression scores were 8.47± 4.26 and 6.66 ± 4.11 in the A2, respectively. The questions concerning education-related details, recent life events and predilection showed that students who faced an important problem in the past six months were significantly more anxious and more depressed compared to others in A2. Students who had suicidal idea had significantly higher scores in HADS ($p < 0.05$). The mean anxiety and depression scores of students in A2 and their comparisons are shown in Table 4.

Table 6: A comparison of three years and anxiety and depression percentages according to cut-off levels of HADS

Score level	2007 - 2008 (A1)		2008 - 2009 (A2)		2009 - 2010 (A3)		p*	P**
	N	%	N	%	N	%		
Anxiety score ≤ 10	117	84.2	68	69.4	77	76.2	0.02	
Anxiety score > 10	22	15.8	30	30.6	24	23.8		
Mean anxiety score	7.35 ± 3.17		8.47 ± 4.26		7.36 ± 4.14			0.05
Depression score ≤ 7	112	80.6	57	58.2	75	74.3	0.00	
Depression score > 7	27	19.4	41	41.8	26	25.7		
Mean depression score	5.03 ± 3.36		6.66 ± 4.11		5.62 ± 3.62			0.00

P* P value according to Chi-square , P** P value according to One-way ANOVA test, HADS: hospital anxiety and depression scale

In A3 students who were not pleased with their career selection and who had the idea to abandon had significantly higher anxiety and depression scores ($p = 0.00$). Students who were predilecting that "never medical career" were also more anxious and more depressed ($p < 0.05$). Table 5 presents A3 results of HADS related to education-related details and recent life events.

Considering cut-off levels of the HADS, 30.6 % of the students were anxious and 41.8% were depressed in A2. A comparison of three years and anxiety and depression percentages according to cut-off levels of HADS are shown in Table 6.

DISCUSSION

In this study we tried to analyze the relationship between anxiety, depression and some demographic, educational and personal factors which were reported as important factors for medical students' stress and well-being in the literature[4,5].

We evaluated medical students during their first three years prospectively. According to cut-off levels of HADS, 15.8, 30.6 and 23.8% of medical students were anxious and 19.4, 41.8 25.7% were depressed in the assessments A1, A2, and A3, respectively (Table 6). In a recent study the overall prevalence of psychological morbidity was 20.9% and was higher among students of basic sciences[17]. Another study reported stress around 40% for both preclinical and clinical students[10]. Eller *et al*[23] noted that 21.9% of the students had symptoms of anxiety, and 30.6% of the students had symptoms of depression. Baldassin *et al*[24] reported depressive symptoms as 38.2% in a cross-sectional study. With HADS overall, 43.7% of students reported anxiety and 19.5% depression in another study[11]. In the study we reported herein anxiety and depression percentages are approximately similar to the recent studies. But our results are below the results of a study that reported a very high prevalence (70%) of anxiety and depression among medical students in Pakistan[16].

In A1, at the beginning of first year at medical school, the mean anxiety score was 7.35 ± 3.17, and the mean depression score was 5.03 ± 3.36. The percentage of anxious and depressed students significantly increased in the second year. It is known that year one students have to adjust to university and new learning environment[12]. The first year of medical school is a major transition, which challenges students' ability to cope with stress[10]. In contrast to the reported increasing prevalence of psychological morbidity between term 1 and term 3, we found that increased anxiety and depression scores in A2 were decreased in A3 approximately to the same level of A1[24]. Although approximately one third of the students in A2 were as depressed as another study reported, students in A1 were not more depressed or anxious than in A2 and A3[11]. Similarly another study also noted that anxiety and depression were not in correlation with study years and age[23]. During the first study year, approximately one-fifth of the students were noted to be suffering anxiety at least weekly in another study[10]. Aproximately one-fifth of the students in A1 were anxious in our study. Uner *et al*[25] did not find any significant difference between the students according to their educational level as first or third-year students. We found a significant increase in depression scores in A2 as mentioned in another study[5]. Similarly, in a study authors noted high levels of anxiety and depression in the 1st and 2nd year students despite less anxiety and depression in 3rd year students[11]. Another study reported a relatively low level of depression, anxiety and stress in year one students and noted year three as a transition point for medical students in respect to negative psychological states[12]. Chandavarkar *et al*[9] also found the highest anxiety, attentional, and depressive symptoms in the third-year medical students. A recent study with Turkish medical students showed a decrease in psychological health between year one and year two[8]. Some researchers suggested that females were more prone to mental health problems consisting of stress, anxiety and depression[23-25]. In general, studies report higher levels of anxiety for female medical students compared to their male counterparts. While Eller *et al*[23] reported a higher frequency of anxiety and depressive symptoms in females, Baldassin *et al*[24] noted a high level of depressive symptoms prevalent among males. But Khan *et al*[16] pointed out that female medical

students experience lower levels of stress as compared to males. In transition periods an elevation of stress level among female students during the first study year, and an increase of male students' stress starting later during the preclinical period with the overload of information was noted in another study[10]. Although we did not find any significant gender difference for anxiety contrary to recent findings reporting female dominance, we found that male students were more depressed in all assessments.

Cost of medical education is an important challenge especially for students from lower income families[26]. Economic problems were also noted in recent studies as the sources of stress in medical students[9,15]. Similarly, students who reported lower family income were significantly more anxious in A1 and more depressed in A1 and A2 in our study. But in A3 students seemed to be adapted to the economic conditions and their HADS scores were like the higher income group.

Informed career selection is a suggested process for a mature, realistic and objective decision making[14,27]. Again our results replicates this suggestion pointing to the importance of informed decision making. Students who got no information about medical education and working conditions were more anxious in A2 and A3. In addition, especially, students who were not informed about working conditions were more depressed in A1 and A2. Of course, it is important to keep in mind the effect of desire for medical career[18]. Besides, there are many contributing factors in decision process such as economic factors, expectations, parental wishes or other external influences *etc*[14,27,28]. Students' reasons for medical career selection and future expectations seems to not have an effect on anxiety scores. External influences in decision process and expecting better economic conditions made students more depressed, especially, in A1 and A2. It may be attributed to the unwillingness and unmet expectations resulting from uninformed decision making.

In addition to medical education medical students face many personal and societal challenges[4]. According to a study, family problems, interpersonal problems, economic problems, career plans, physical health, medical lecture workload and poor academic performance increase the pressure on medical students[15]. The most common sources of stress were noted to be related to academic and psychosocial concerns. The most important and severe sources of stress were staying in hostel, high parental expectations, vastness of syllabus, tests / exams, lack of time and facilities for entertainment *etc*[17]. Stressful personal life events such as illness or death of family members *etc* were found to be related to students' wellbeing[5]. The main components of the students' lives are their education, their families and their intimate partners and the presence of a negative event was found to increase the risk of having a mental problem[25]. In a recent study, students who experienced negative personal life events did not have a higher frequency of burnout than students who did not experience a negative personal life event. But personal characteristics, learning environment and personal life events were all found to be independently related to student's burnout[4]. The number of negative personal life events in the last 12 months were also in correlation with the risk of burnout[5]. Those who had suffered any negative life events, such as failing an examination, death of a parent and other social burdens, were more depressed than those who had experienced positive life events[11]. When students were asked about the most distressing event in the last year, nearly half of them reported educational problems such as failing the class or failure to study in a faculty of their preference, loss of a family member or breaking up with their partner because of an infidelity or a quarrel[25]. Moreover, the level of dissatisfaction in social activities was associated with all psychological test scores for medical students. In addition, romantic relationships and anxiety about the future were determined as being the other factors associated with psychological test scores[8]. Medical students in Hong Kong reported a higher level of psychological morbidity with concerns including examinations, stress, career, adjusting to the new medical curriculum and commitment to the course[12]. Loss of relative was also one of the predictors of depression and anxiety among students. Students who had lost a close relative in last one year were 3.4 times more likely to be depressed and suffer from anxiety as compared to those who did not experience such a loss[16]. Similarly, in this study we found that students who faced an important problem in the past six months were significantly more anxious and more depressed in A2 and A3. But when it comes to the contributing factors although problems about education and school were the most reported, according to HADS scores these were the least factors worsening their well-being. With these results we could not claim that education related factors were significant contributing factors for anxiety and depression of medical students as noted before[15]. A large proportion of students in both clinical and basic science have potential psychological problems mainly related to academics and psychosocial concerns[17]. High academic achievement was noted to have a positive effect on the mental health of students[25]. There are both positive and negative correlations between academic achievement and anxiety and depression in medical students, regarding differing levels of severity of anxiety or depression[15]. Similarly, problems related to school in the past six months were mentioned mostly but the HADS scores were in contrast in this study. These results maybe attributed to different factors unique to our faculty. In the faculty of Medicine in Meram, every year, two-third of the all students in the first three years got scores higher than 80 points out

of 100 and were awarded a pass without the final exam and just 8 to 15 students failed. Students assigned school problems but we cannot say that these are the problems which are related to academic performance. We should ask another question to get the details of what they mean by problems about school. Perhaps, an open ended question should detail it. Because we eliminated the failed ones and because of the high scores that our students have we may say that these "problems about school" point toward some different issues other than exam scores.

Our results were in favor of a study reporting that besides educational demands, social and friendship-related factors are reasons for psychological disturbance in university students[8]. In addition, although students in A2 and in A3 who had suicidal idea were more anxious and depressed, HADS scores of students who reported school problems were not higher than others. But school problems were among the prominent reasons for suicidal idea. In A2, the time of suicidal idea was reported as "more than one year before" which points to a time before beginning of medical education. But in A3 students, who had suicidal idea in the past one year, had higher scores in HADS specific to second academic year in medical education. But the higher HADS scores with suicidal idea resemble the suggestion that elevated anxiety or depression might each be associated with increases in the frequency of suicidal thoughts, while elevations of both together convey additional risk[29].

Dissatisfaction with the learning environment was noted to be related to student's burnout varying between preclinical and clinical students[4]. For this study we tried to determine the dissatisfaction with questions about pleasure with the career, the idea of abandon, reason for the idea of the abandon and predilection. Students who were not pleased with their medical career and who had the idea of abandon had significantly high scores in HADS in A2 and A3. But idea of abandon was mostly depending on problems other than school. In a recent study almost half (48.8%) of the anxiety disordered participants reported leaving school prematurely[30]. Naturally, willingness and desire are important in well-being of medical students as in other careers[18,25]. When students were asked for their predilection three of four of the students were still longing for being a doctor. The recent, especially the ones who predilected that "never medical career" were significantly more anxious and more depressed. Once more we all should think about informed decision making and willingness before beginning medical education as reported in the literature[18,27]. As expected, enrollment in a non-preferred faculty has negative effects on mental health[25]. Career advice should be available at all stages of medical training for this kind of students.[12]

CONCLUSION

This paper mainly focuses on students' psychological well-being in terms of different variables and academic years. With this study, we demonstrated the changing profile of anxiety and depression of the medical students prospectively. It is important to gather data about the psychosocial changes made by first-year medical students during their education in order to make more informed decisions about education and therapeutic programs designed to promote the personal development of each student[2]. Our results indicate that especially in the second academic year, medical students were at a great risk. The results of this study also suggest that medical education itself is not the only stress for medical students. Other problems they have may be worsening their psycology more. The importance of delivering occupational counseling services and informed decision are once more determined[12,25,27]. It is known that student distress influences professional development[4]. Our findings also supports the idea that screening medical students for anxiety and depression may be helpful in identifying medical students who are at risk for co-morbidities and suicide risk[8,9,24]. Psychological worsening needs social and psychological support to improve the quality of life for these medical students and would help them to cope with the stressors at various stages of their medical ed ucation[7,10,12,16,17]. In correlation with the recent reports personal, familial and educational factors seem to contribute to students' anxiety and depression. Personal life events with educational problems contributes to the worsening of their psychology[4,5]. However, further research is needed to determine the degree to which medical education *per se* is contributing to anxiety and depression and its relationship with academic performance.

LIMITATIONS

Our study has some strength and some limitations. To the best of our knowledge, this is one of the limited prospective studies about anxiety and depression in medical students. A self-reported questionnaire may be called biased, but the HADS questionnaire was a validated one and it was tested and used in a lot of studies and many times in various groups and in different languages. However, it cannot be compared to psychiatric interviews. We only screened for symptoms of anxiety and depression but it is not possible to say that these students had anxiety and depression disorders. Another limitation is not asking a question to get the details of what they mean by problems about school. *Via* an open ended question, we should have detailed it. Because the questionnaires were anonymous, we are unable to determine the psychological profile of each student and we could not know the students at risk. The results of this study

only reflect the students of this institute and it cannot be generalized to the other institutions. The voluntary participation may be another factor which may call to bias but the number of students who volunteered and participated in each year was considerably high.

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Original Article

Comparison of Changes in Body Image of Patients with Renal Calculi Treated by Pyelolithotomy or Percutaneous Nephrolithotomy

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ABSTRACT

Objective: To compare changes in body image of patients who had pyelolithotomy (PYL) or percutaneous nephrolithotomy (PNL) for kidney stones
Design: Prospective, descriptive study
Setting: Elazig Education and Research Hospital, Turkey
Subjects: A total of 69 patients, who had PNL or PYL done for renal stones, were evaluated, prospectively.
Interventions: Patients were divided into two groups: PNL (39 patients) and PYL (30 patients). Body dismorphic disorder scale (BDDS) was used to measure body image changes of these patients before, one and six months after the operation. The patients were questioned and their answers were noted. BDDS score was calculated according to the answers.
Main Outcome Measures: Mean BDDS scores between the two groups were statistically compared by t-test method
Results: The difference of mean BDDS scores between two groups before the operation, and six months after the operation was not statistically significant ($p > 0.4$ and $p > 0.4$ respectively). However, mean BDDS scores one month after the operation were significantly higher in PYL group and perception of body image was worse ($p = 0.01$).
Conclusion: In early postoperative period, perception of change in body image was significantly worse in the PYL group. However, in late postoperative period, there were no significant differences between the two groups of patients. For these reasons, we consider that the changes in body image should not be a determining factor for selecting the surgical approach.

KEY WORDS: body image, percutaneous nephrolithotomy, pyelolithotomy

INTRODUCTION

The main factors that determine the treatment method in renal stone are location, size, number of stones and structure and anatomy of the urinary tract[1-2]. Main surgical methods for the treatment of kidney stones are ureterorenoscopy (URS), pyelolithotomy (PYL) and percutaneous nephrolithotomy (PNL). After its first application in 1976, and by the development in instrumentation, PNL has become a standard method of care in surgical treatment of kidney stones, with low morbidity, short convalescence and low costs[3]. For these reasons, open surgical procedures such as PYL are preferred only in selected cases in developed countries. Despite this evidence, open kidney surgery is widely performed in many urology centers so far. Body image changes as evaluated by the patient after surgery, is an important factor to be considered for choosing the surgical technique. Body image is the individual's perception of his own body and his own evaluation of positive and negative feelings against his own body parts and their functions[4].

PYL, which leaves a large scar on the patient's body, can be considered to cause significant changes in body image, while PNL which leaves a very small scar, can be thought to cause the least change in body image. However, effects of the preferred surgical method on body image, is an issue to be examined separately for each community because of different value judgments of societies. In this study, we compared body image and surgical techniques in patients who had PNL or PYL for treatment of kidney stones.

SUBJECTS AND METHODS

Sixty-nine patients, who had PNL or PYL for renal stones, were evaluated in this study. Out of the 69 patients, 39 (male / female: 29/10), hadPNL, while 30

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Table 1: Body Dismorphic Disorder Scale (Circle the best choice describing the patient)

Q. No.	Questions and Choices	Value
1	Time spent on thoughts about body disorders (How much time do you spent on thinking about your body disorders in your daily life?)	
	A. No time	0
	B. Only a little (less than an hour in a day or thoughts arising rarely, not more than 8 times a day)	1
	C. Moderate (1 - 3 hours in a day or thoughts arising frequently, more than 8 times a day but these thoughts are not available for most time in a day)	2
	D. Intense (more than 3 hours in a day, but not more than 8 hours or thoughts arising very often, more than 8 times and most of the time in a day)	3
	E. Excessive (more than 8 hours or thoughts arising nearly always, too much to count and an hour is hardly spent without these thoughts)	4
2	To be blocked owing to thoughts about body disorders (How much do body defects hinder your daily life?)	
	A. Never	0
	B. Only a little (hinders social and professional functions slightly but does not hinder general functions)	1
	C. Moderate (hinders social and professional functions but still can be handled)	2
	D. Intense (hinders social and professional functions on an important scale)	3
	E. Excessive (making you out of work)	4
3	Distress related to thoughts about body disorders (On what scale do body defects lead to anxiety in your daily life?)	
	A. Never	0
	B. Only a little, rarely but and not disturbing	1
	C. Moderate, often and disturbs but still can be handled	2
	D. Intense, very often and disturbing	3
	E. Excessive, nearly always and disturbing as much as to hinder your activities	4
4	Resistance to thoughts about body disorders (On what scale do you resist to body disorders as if there were nothing?)	
	A. Always struggling to resist or symptoms are too little to resist	0
	B. Trying to resist most of the time	1
	C. Making some effort to resist	2
	D. Submitting to these thoughts without trying to control but doing this unwillingly	3
	E. Submitting to these thoughts completely and willingly	4
5	Control level of thoughts related to body disorders (On what scale can you control your thoughts when your body imperfections come to your mind?)	
	A. Total control	0
	B. Control on a great scale (being able to stop these thoughts or directing them to something else)	1
	C. Moderate control (sometimes being able to stop these thoughts and direct them to something else)	2
	D. Little control (rarely being able to stop these thoughts but hardly changing their directions)	3
	E. No control (experiencing without your own will, rarely changing the direction of these thoughts only for a moment)	4
6	Time spent on activities related body disorders (How much time do you spend on hiding your body disorders in your daily life?)	
	A. Never	0
	B. Only a little (spending less than one hour with these activities or rarely being busy with these activities, not more than 8 times a day)	1
	C. Moderate (from 1 - 3 hours in a day or more than 8 times a day but not being busy with these activities for most of the time in a day)	2
	D. Intense (more than 3 hours in a day but not more than 8 hours or being busy with these activities very often, more than 8 times a day and these activities are not carried out for most of the time in a day)	3
	E. Excessive (more than 8 hours in a day or nearly always being busy with these activities, too much to count and hardly an hour is spent without these	4
7	Being blocked owing to the activities related to body disorders (On what scale do body disorders affect the activities in your daily life?)	
	A. Never	0
	B. Only a little, slightly hindering social and professional activities but general functions are not disturbed	1
	C. Moderate (social and professional functions are definitely hindered but still can be handled)	2
	D. Intense, disturbing social and professional functions on an important scale	3
	E. Excessive, making you out of work	4
8	Being forced as a result of activities related to body disorders (On what scale do you feel uncomfortable when your body disorders affect your daily life activities?)	
	A. Never	0
	B. Only a little, feeling a slight discomfort when your behaviors are hindered during the activity	1
	C. Moderate, increasing discomfort when your behaviors are hindered but still can be handled	2
	D. Intense, increasing discomfort on a great scale during your activities or your behaviors are hindered	3
	E. Excessive, discomfort increasing as a result of interference during the activity related to body disorders	4

9	Resistance to compulsions (On what scale do you resist to difficulties resulted from body disorders?)	
	A. Always making an effort to resist or symptoms are too little to require any effort	0
	B. Trying to resist for most of the time	1
	C. Making a little effort to resist	2
	D. Submitting to these difficulties without trying to control but making this without intention	3
	E. Totally submitting to difficulties related to body disorders willingly	4
10	Control level of compulsive behaviors (On what scale can you control yourself against forcing situations resulting from body disorders in your daily life?)	
	A. Total control	0
	B. Control on a great scale, feeling pressure to realize activity but generally being able to control with your own will	1
	C. Moderate control, feeling a strong pressure to realize activity but being able to control with difficulty	2
	D. Slight control, feeling a great pressure to realize activity, having to complete but hardly being able to postpone	3
	E. No control, being forced to realize activity without your own will in an excessively strong manner and rarely realizing activity only for a moment	4
11	Insight: (On what scale do you consider about this body disorders as logical when you question the condition?	
	A. Perfect insight, totally logical	0
	B. Good insight, accepting absurdity and excessiveness of thoughts and behaviors but seeming not totally convinced about the fact that there is nothing to worry about this condition other than distress	1
	C. Moderate insight, accepting excessiveness and absurdity of your thoughts and behaviors but hesitating, possibility of having some unreal fears but without any stable belief	2
	D. Weak insight, claiming that thoughts or behaviors are logical or excessive	3
	E. No insight, definitely believing that thoughts and behaviors are logical and not being convinced with the contrary evidences	4
12	Avoidance: (On what scale do you avoid doing your daily life activities because of your body disorders?)	
	A. No avoidance	0
	B. Slight, only a little avoidance	1
	C. Moderate, slight avoidance, avoidance is clear	2
	D. Avoidance on a great scale, avoidance is clear	3
	E. Excessive, very prevalent avoidance, patient avoiding almost all the activities	4

(male / female: 23/7) had PYL. Patients who had an additional factor that may affect the body image, such as previous surgery or claudication, were excluded from the study. Patients who accepted and signed our study protocol and were communicable, were chosen for the study.

Patients were divided into two groups as PNL and PYL. Patients' perceptions of body image was assessed with the body dysmorphic disorder scale (BDDS, Table 1). Prior to this study, the BDDS was tested in patients who had had an ileal conduit or an ileal neobladder[5]. Patients were assessed for BDDS, consisting of 12 questions, before surgery, at one month and at the end of six months after the surgery. BDDS form was completed by the same doctor. The answers to each question were scored from 0 - 4 points on a subjective scale[5] (Table 1). Higher BDDS score showed the patient's poor perception of body image.

Results were analyzed with SPSS for Windows®. Means and standard deviations were determined. Mean scores between the two groups of patients were compared using the t-test. A p-value lower than 0.05 was considered as statistically significant.

RESULTS

Mean ages of the patients were 43.48 ± 9.37 years (minimum: 28 years - maximum: 62 years) in the PNL group and 44.96 ± 8.73 years (minimum: 29 years - maximum: 61 years) in the PYL group. There were no statistically significant difference between two groups in terms of age ($p > 0.2$).

In the PNL patients, average BDDS scores before, at first month and at sixth months after the surgery were 13.12 ± 4.40, 14.79 ± 4.09 and 13.48 ± 4.33, respectively. In the PYL group the average BDDS scores before, at the first month and at the sixth months after the surgery were 13.86 ± 4.47, 17.03 ± 2.84 and 14.23 ± 3.98 respectively (Fig. 1). There were no statistically significant difference between the two groups in terms of BDDS scores before and at six months after surgery ($p > 0.4$ and $p > 0.4$, respectively). However BDDS scores were significantly higher and perception of body image was significantly worse in the PYL group ($p = 0.01$) (Table 2).

Table 2: Number of patients, mean BDDS scores and p-values (t-test) for two types of operation.

	Operation type (N = 69)		p-value
	PNL n = 39 (57%)	PYL n = 30 (43 %)	
Mean BDDS score			
Pre-operative	13.12 ± 4.40	13.86 ± 4.47	> 0.4
1st month	14.79 ± 4.09	17.03 ± 2.84	0.01
> 6 months	13.48 ± 4.33	14.23 ± 3.98	> 0.4

PNL: percutaneous nephrolithotomy; PYL : pyelolithotomy

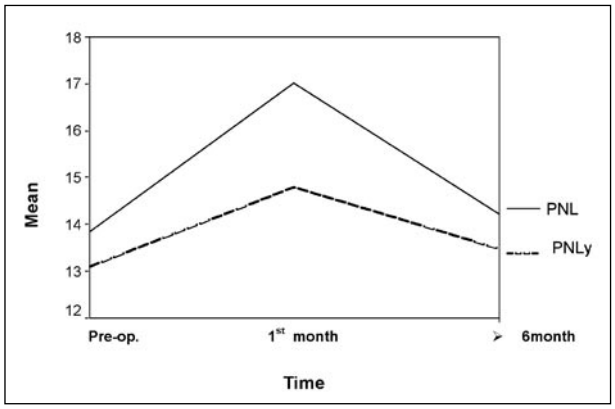

Fig 1: Mean BDDS scores of PNL and PYL patients

In patients who had PNL, BDDS mean points for pre-operative, post-operative at the first month and post-operative after six months were compared and found to be not statistically significant ($p > 0.08$ Vs $p > 0.7$) In patients who had PYL, BDDS mean points for pre-operative, post-operative after six months and were not statistically significant ($p > 0.7$). However, BDDS mean point was considerably higher and the body image perception was more negative between the groups at the post-operative first month ($p = 0.002$) (Table 3).

Table 3: The comparison of preoperative and postoperative BDDS median scores and p-values in PNL and PYL groups

Operation type	Mean BDDS score, Pre-op. and 1st month	p- value	Mean BDDS score, Pre-op. and > 6 months	p- value
PNL	13.12 ± 4.40 14.79 ± 4.09	0.087	13.12 ± 4.40 13.48 ± 4.33	0.718
PYL	13.86 ± 4.47 17.03 ± 2.84	0.002	13.86 ± 4.47 14.23 ± 3.98	0.739

BDDS: Body dismorphic disorder scale

BDDS mean points at the pre-operative, post-operative first month and post-operative after six months were compared between the male and female patients in the PNL group and were not statistically significant (p values were as follows: > 0.1, > 0.07 and > 0.5, respectively). Additionally, there was no difference between male and female patients who had PNL when BDDS mean points for pre-operative and post-operative at six months were compared ($p > 0.1$ and $p > 0.4$, respectively). However, post-operative first month BDDS mean point for the male patients who had PYL was considerably higher and the body image perception was more negative than females ($p = 0.005$).

The BDDS mean points for pre-operative, post-operative first month and post-operative more than six months were compared for the younger patients Vs the older patients who had undergone PYL. There was no significant difference (p-values were > 0.8, > 0.05 and > 0.9, respectively). Moreover, there was no difference in older patients Vs younger patients who had undergone PNL when the BDDS mean points for pre-operative and post-operative more than six months were compared ($p > 0.1$ and $p > 0.1$). However, post-operative first month BDDS mean point of the younger patients were significantly higher and the body image perception was more negative than older patients withPNL ($p = 0.006$).

DISCUSSION

Urinary tract stone disease is the third most common pathological condition in the urinary system, coming after urinary infections and prostate disease. In recent years, there has been a great progress in the medical treatment of urinary stone disease[3]. However, the majority of these patients still have a high rate of indication for surgical treatment. The aim of treatment in urinary tract stone disease, at the acute stage, is to recover from the pain and discomfort for the patient. On the other hand, the ultimate aim should be the clearance of urinary tract from stones as far as possible and to prevent new stone formation or growth of existing stone[3]. Providing high quality of life should be a target in this group of patients.

By many changes in the view or function of any body part, body image is changed and the patient can see himself as completely different. Body image can vary by some reasons such as hormonal changes, illness, disability, injury, surgery, radiotherapy and chemotherapy[4]. In this study, patients with additional pathology that could adversely affect the body image were excluded.

We found no study comparing body images after PNL and PYL in the English literature. We found few studies that compared changes in quality of life and body image in different types of urinary diversion. Hart and his colleagues reported no difference in body image changes of the patients with different types of urinary diversion[6]. However, some studies reported some differences in body image for different techniques of urinary diversion[7-8].

In our study, the change in body image in the early post-operative period was significantly different between PNL and PYL groups and average BDDS score was higher in PYL group. However, mean BDDS scores were not significantly different between two groups by age and sex at sixth months after the operation. This result may be due to the adaptation of patients to changes in body image at the late period.

In previous studies, it was normal to expect different results about the impact of surgical method on body image. This is because in countries and societies and even within the same society, there are many differences in socio-economic status, life outlook, customs and way of life. Therefore, we recommended

that each society should develop its own models and make research according to these models.

CONCLUSION

In our study, we compared patients who underwent PNL and PYL in terms of body image changes. There was no statistically significant difference between two groups before and at sixth months after the surgery. However, there was significant difference at one month after surgery and changes in body image were higher in PYL group than PNL. Body image perception was worse in PYL group in early post-operative period. Although body image changes were higher in early post-operative period in PYL group, in which the incision scar was evident, the difference disappeared in late period. For these reasons, we consider that observed changes in body image should not be a determining factor for selecting the surgical method in patients with renal calculus.

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Original Article

The Prevalence and Route of Delivery of Prolonged Pregnancies

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ABSTRACT

Objective: To evaluate the prevalence, rate and indications for cesarean deliveries in prolonged and post-term pregnancies
Design: Prospective descriptive cross-sectional study
Setting: Department of Obstetrics and Gynecology, University Hospital Amir, Semnan, Iran.
Subjects: One hundred and sixty-four cases of prolonged pregnancy were encountered during the study period from September 2009 to September 2010. Data regarding total deliveries, number of prolonged pregnancies and cesarean delivery were gathered and the prevalence of prolonged pregnancy, the cesarean delivery rate and the indications for cesarean deliveries evaluated.
Main Outcome Measures: Prevalence of prolonged pregnancies and cesarean delivery rates
Intervention: Delivery and cesarean section
Result: Total deliveries during this period were 1157. Forty-one and 13 deliveries were beyond 41 weeks (prolonged pregnancy) and 42 weeks (post term pregnancy) respectively. The prevalence of prolonged pregnancy and post term pregnancy was 3.5 and 1.12% respectively. The cesarean delivery rate for prolonged and post-term pregnancy were 31.7 and 38.46% respectively. The most common indications for cesarean deliveries were failure to progress and meconium staining of amniotic fluid.
Conclusion: The prevalence of prolonged and post-term pregnancy was low and the incidence of cesarean section was high in these cases.The most common indications for cesarean section were dystocia (failure to progress) and meconium staining of amniotic fluid .

KEY WORDS: cesarean delivery, post-term, prolonged, pregnancy

INTRODUCTION

Prolonged pregnancy refers to a pregnancy that has extended to beyond 42 weeks (294 days) gestation[1]. This definition is endorsed by the American College of Obstetricians and Gynecologists (ACOG), the World Health Organization (WHO) and the International Federation of Gynecology and Obstetrics. In view of more recent perinatal mortality data, it would be reasonable to conclude that prolonged pregnancy should be defined as gestational age at birth greater than or equal to 41 weeks of gestation[2]. The etiology of prolonged pregnancy is unknown. It is associated with an increased adverse outcome in both the fetus and the mother[1]. The incidence of prolonged pregnancy is estimated as 4 - 19% at 42 weeks gestation and 2 - 7% at 43 weeks of gestation[2].

The prevalence of post-term pregnancy depends on the population characteristics including such factors as nulliparity, a prior post-term pregnancy and genetic predisposition. The main complications associated with pregnancy beyond 40 and 41 weeks of gestation are stillbirth, perinatal mortality and morbidity and increased risk of cesarean delivery[3].

Obesity, maternal age 30 - 39 years and 40 years or older are others risk factor of prolonged pregnancy[4].

As pregnancy progresses beyond 40 weeks of gestation, the risks of maternal peripartum complications increase[5] and the rates of cesarean delivery increase with increase of gestational age[6,7]. Labor induction, prolonged second stage of labor, forceps use and operative delivery are other maternal complications of prolonged pregnancy beyond 41 weeks[8]. In this study, the prevalence rate of cesarean delivery and the indications for cesarean in prolonged pregnancy were evaluated.

SUBJECTS AND METHODS

A prospective descriptive cross-sectional study was carried out on all prolonged pregnancy cases encountered in the Semnan University Hospital Amir, Semnan, Iran from September 2009 to September 2010.

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All deliveries during this period were recorded and every case that had gestational age beyond 40 weeks was enrolled in the study. The duration of gestational age was determined based on the date of the last menstrual period or ultrasound between 8 - 28 weeks of pregnancy. The patients who had uncertain date or no ultrasound scanning in the mentioned period were excluded.

Pregnancies beyond 41 weeks were considered as prolonged pregnancy. The prevalence of prolonged pregnancy, the cesarean delivery rate and indications for cesarean section were evaluated.

Data are expressed as percentages in the text and tables and compared using the chi square test. A p-value less than 0.05 was considered significant. Statistical analyses were performed using statistical package for social medicine (SPSS version 16/0)

RESULTS

The mean age of the study group was 28 ± 5.8 years. The total number of deliveries during this period was 1157 out of which 164 cases (14.17%) were beyond 40 weeks. Forty-one cases of prolonged pregnancy (beyond 41 weeks) and 13 cases of post-term pregnancy (beyond 42 weeks) were recorded. Therefore, the prevalence of prolonged pregnancy was 3.54% and the prevalence of post-term pregnancy was 1.12%. There were 29 cases (70.73%) between 41 - 42 weeks, 10 cases (24.3%) between 42 - 43 weeks, one case (2.43%) between 43 - 44 weeks and one case (2.43%) longer than 44 weeks of gestation. Eighty cases (42%) were primipara and 84 cases (51%) were nullipara (p = 0.000).

Table 1: Indications for cesarean delivery in pregnancy beyond 40 weeks

Causes	n	%
Failure to progress	22	32.08
Meconium staining	17	25.37
Repeat cesarean	11	16.41
Fetal distress	6	8.95
Meconium + fetal distress	4	5.97
Breech presentation	2	2.98
Other cases	5	7.46
Total	67	100.00

Ceasarean section was the mode of delivery in 67 cases (40.11%) beyond 40 weeks. The most common indications for cesarean section in pregnancy beyond 40 weeks were failure to progress (22 cases, 32.8%) and meonium staining of amniotic fluid (17 cases , 25.37%). Repeat cesarean section (11 cases ,16.41%), fetal distress (6 cases , 8.95%), meconium + fetal distress (4 cases , 5.97%) and breech presentation (2 cases , 2.98%) were other indications for cesarean deliveries (Table 1).

In 18 cases (43.90%) where the pregnancy was beyond 41 weeks, the mode of delivery was cesarean section. The most common indication for cesarean delivery was failure to progress (4 cases ,22.22%). meconium staining of amniotic fluid (4 cases , 22.22%), repeat cesarean (4 cases , 22.22%), fetal distress (3 cases ,16.66%), meconium staining + fetal distress (1 case , 5.55%) and breech presentation (1 case , 5.55%) were other indications for cesarean delivery (Table 2).

Table 2: Indication of cesarean delivery in prolonged pregnancy

Causes	n	%
Failure to progress	4	22.22
Meconium staining	4	22.22
Repeat cesarean	4	22.22
Fetal Distress	3	16.66
Meconium + fetal distress	1	5.55
Breech presentation	1	5.55
Other cases	1	5.55
Total	18	100.00

DISCUSSION

There are different prevalence rate for prolonged pregnancy in different studies. Roos *et al*[9] reported 8.94% as prevalence rate for post- term delivery but in our study it was 3.45%. Brennan *et al*[10] found 3.5% -14% prevalence for pregnancy beyond 42 week and Torricelli *et al* reported 7% prevalence[3]. Both figures are higher than our rate. Divon *et al*[2] stated 4 to 19% as prevalence rate for post-term pregnancies but in our study this was 1.12%.

Longer gestation at term is associated with increased risk of cesarean birth[11] and maternal complications such as cesarean delivery (12.3 - 21.6%), operative vaginal delivery and maternal hemorrhages are highest in post-term pregnancy and lowest at 39 weeks[12].

The cesarean delivery rate in cases beyond 41 weeks was 43.90% in our findings, whereas the cesarean section rate in Hermus *et al* study was 12.5 - 13.6%[13]. Chanrachakul *et al* reported 21.6 - 26.6% cesarean delivery rate in pregnancies beyond 41 weeks plus three days which is about half that of our study[14].

Our study revealed that the most common indications for cesarean delivery in prolonged pregnancy were dystocia (failure to progress) and meconium staining of the amniotic fluid. Meconium staining of the amniotic fluid is a common occurrence and increases with gestational age from 7 to 25% of term deliveries to 23 to 52% after 42 weeks. Thick meconium staining of amniotic fluid is associated with poor perinatal out come[15]. Therefore, cesarean delivery for prevention of fetal complication is justified. Based on our findings the occurrence of meconium staining

of amniotic fluid was 7.3% in prolonged pregnancy and 15.38% in post-term pregnancy.

The overall risk of prompt cesarean section for fetal concern is 3.1% and the risk exceeded 20% in patients with post-term pregnancy[16]. Umbilical cord compression due to oligohydramnios is the principal mechanism of intrapartum fetal distress in post term pregnancy[17]. The cesarean section rates of post-term pregnancy due to fetal distress were 16.6% in our study.

CONCLUSION

The prevalence of prolonged pregnancy and post-term pregnancy was lower whereas the cesarean section rate higher in this study as compared to figures reported in the literature. The most common indications for cesarean section were dystocia and meconium staining of the amniotic fluid.

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Original Article

Determining the Effect of Sufentanil on Propofol Injection Pain

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ABSTRACT

Objectives: Propofol is a general anesthetic. Its most important disadvantage is pain on injection. Our aim was to evaluate the effectiveness of sufentanil on propofol injection pain (PIP).
Design: Case control randomized double-blind study
Setting: Anesthesia department of Selcuk University Meram Medical School , Turkey
Subjects: A total of 160 adults, 18 to 65 years, ASA I-II patients, scheduled for operations under general anesthesia, were enrolled in this study. A 22-gauge intravenous (IV) catheter was inserted into a vein on the dorsum of the hand. Patients were randomly allocated to one of four groups to receive either saline or 0.5, 1, 2 mcg sufentanil in 2 ml volume. Thirty seconds after the intravenous (IV) injection of the pretreatment drug, 5 ml of 1% propofol at room temperature (Fresenius Kabi, Hamburg, Germany) was injected IV at rate of 0.5 ml/sec. Pain was assesed verbally and scored as none (0), mild (1), moderate (2), severe (3).
Interventions: Prior injection of sufentanil or placebo
Main Outcome Measures: Severity of PIP
Results: Demographic data were comparable among four groups. Sufentanil at 1 and 2 mcg doses significantly decreased pain incidence when compared to the saline group ($p < 0.05$). Sufentanil 0.5 mcg had no effect ($p > 0.05$). Although 2 mcg sufentanil decreased the incidence of PIP more than 1 mcg, there was no significant difference between these groups ($p > 0.05$).
Conclusion: Sufentanil at one and 2 mcg doses reduced the incidence and severity of PIP

KEY WORDS: general anesthesia, pain, propofol, sufentanil

INTRODUCTION

Propofol is a frequently used intravenous (IV) anesthetic for induction of anesthesia and for sedation in daycase surgery. The most important disadvantage of propofol is injection pain, which is reported in 28 - 90% of patients[1].

Many different methods have been proposed to reduce the incidence and severity of this adverse effect of propofol. Pretreatment with alfentanil[2], use of fentanyl[3], local anesthetics[4], metoclopramide[5], tramadol[6], ketamine[7], ondansetron[8], addition of lidocaine[9,10], alfentanil[11] ephedrine[12], granisetron[13], and injection of propofol into a large antecubital vein or into a freely flowing intravenous (IV) line, are the techniques described for prevention of propofol injection pain (PIP) .

Fentanyl, remifentanil, alfentanil and sufentanil can provide analgesia and assist anesthetic effects when used as presurgical medication, induction or maintenance agents, for postsurgical pain relief and neurolept and neuroleptanalgesia and as supplements to regional anesthesia. Opioids are also reported to be effective in preventing PIP[3,10,11]. Sufentanil is a selective μ receptor agonist, 5-10 times more effective analgesic than fentanyl and with a high safety[14].

However, there are few studies in literature that report sufentanil analgesic effect on PIP. In this study we tried to evaluate effectiveness of sufentanil, in prevention of PIP.

SUBJECTS AND METHODS

Ethics Committee approval was obtained from Selcuk University Meram Medical Faculty. All patients gave their informed and written consent. A total of 160 adult, aged between 18 to 65 years, ASA physical status I-II patients, scheduled for operations under general anesthesia, were enrolled into this randomized, double-blind study conducted in 2006 at the anesthesiology department of Meram Medical School of Selcuk University. Patients with

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a history of neurologic or psychiatric disease, difficulty with communication, analgesic and / or sedative administration, history of renal or hepatic insufficiency, thrombophlebitis and hypersensitivity to the study drugs were excluded from the study.

On patient arrival in the operating room without any premedication, a 22-gauge intravenous (IV) catheter was inserted into a vein on the dorsum of the hand. Patients were monitored with electrocardiography, pulse oximetry (oxygen saturation), and non-invasive blood pressure. All infusion fluids were 0.9% normal saline at a rate of 500 ml/h. The study subjects were randomly allocated to one of four groups to receive either saline, 0.5, 1 or 2 mcg sufentanil in 2 ml volume. Thirty seconds after the intravenous (IV) injection of the pretreatment drug, 5 ml of 1% propofol at room temperature (Fresenius Kabi, Hamburg, Germany) was injected IV at a rate of 0.5 ml/sec. Pain was assesed verbally and scored as none (0), mild (1), moderate (2) and severe (3). Any spontaneous complaints of pain were noted. If there were no spontaneous complaints, patients were asked about pain 30 seconds after the propofol injection. Observations were noted by an independent observer.

Induction of anesthesia was performed in all patients with propofol upto 2.5 mg/kg, 0.6 mg/ kg atracurium and 1 - 2 mcg sufentanil. Anesthesia was maintained with nitrous oxide 50% and sevoflurane 2 - 2.5% in oxygen.

Any excitation during induction and reactions such as hypotension, nausea, vomiting or flushing were recorded.

Statical analysis

Statistical analysis was carried out using SPSS for WINDOWS software program version 15.0 (SPSS, Chicago, IL). The Mann Whitney-U test was used to analyze the results of the patients' subjective assessment of pain. A p-value less than 0.05 was considered statistically significant. Differences between scores from the saline group and the other groups were estimated as 1.5 and with a 0.05 α error (two- sided) the required sample size was 40 per group yielding a power higher than 90%.

Table 1: Characteristics of the patients (mean ± SD)

Patient Characteristics	Group 1	Group 2	Group 3	Group 4
Sex (F/M)	17/23	21/19	19/21	18/22
ASA I/II	21/19	19/21	20/20	21/19
Age	37.8 ± 12.05	38.4 ± 13.10	34.08 ± 12.06	33.03 ± 11.04
Weight (kg)	70.2 ± 11.03	70.7 ± 12.08	70.97 ± 11.05	70.55 ± 12.7

RESULTS

The study included 160 patients. Demographic data were comparable among four groups (Table 1). The patients did not experience any pain or discomfort during study drug injection.

The overall pain incidence was 92.5% in the saline group and 70% in all study groups. When we compared the saline group and sufentanil groups, sufentanil decreased PIP incidence significantly ($p < 0.05$). Pain incidence was 95% in 0.5 mcg sufentanil group, 77.5% in 1 mcg sufentanil group and 45% in 2 mcg sufentanil group. Sufentanil at 1 and 2 mcg doses significantly decreased PIP incidence when compared to the saline group ($p < 0.05$, Table 2). 0.5 mcg sufentanil had no effect on PIP incidence ($p > 0.05$, Table 2). Although 2 mcg sufentanil decreased PIP incidence much more than 1 mcg group, the difference was not significant ($p > 0.05$). Moderate and severe pain incidence was 2-8 (5 - 20%) in Group 3 and 4-4 (10%-10%) in Group 4. It was significantly decreased when compared to Group 1 and 2 ($p < 0.05$, Table 3).

Table 2: Distribution according to reported pain by the patient

Status of Pain	Group 1 %	Group 2 %	Group 3 %	Group 4 %
No Pain	7.5	5	22.5	55
Pain	92.5	95	77.5 *	45 **

*$p < 0.05$ compared to Group 1 and 2
** $p < 0.05$ compared to Group 1 and 2

Table 3: Distribution of the patients according to intensity of the pain

Intensity of pain	Group 1 (N = 40) n (%)	Group 2 (N = 40) n (%)	Group 3 (N = 40) n (%)	Group 4 (N = 40) n (%)
No Pain (VAS 0)	3¥ (7.5)	2¥€ (5.0)	19* (47.5)	22** (55.0)
Mild Pain(VAS 1)	6 (15.0)	11 (27.5)	11 (27.5)	10 (25.0)
Moderate Pain(VAS 2)	12 (30.0)	14 (35.0)	8*¥ (20.0)	4¥¥ (10.0)
Severe Pain(VAS 3)	19 (47.5)	13 (32.5)	2€ (5.0)	4€€ (10.0)

*$p < 0.05$ compared to Group 1 and 2, ** $p < 0.05$ compared to Group 1 and 2, *¥ $p < 0.05$ compared to Group 1 and 2, ¥¥ $p < 0.05$ compared to Group 1 and 2, € $p < 0.05$ compared to Group 1 and 2, €€$p < 0.05$ compared to Group 1 and 2, ¥ $p < 0.05$ compared to Group 3 and 4, ¥€ $p < 0.05$ compared to Group 3 and 4

DISCUSSION

Propofol is a 2,6 disopropyl phenol and like all phenols it irritates the skin , mucous membranes and venous intima. PIP is still a common problem and the ideal method for its prevention is still controversial. Among 33 clinical problems, PIP has been seventh in the list, when both clinical importance and frequency were considered[15]. There are a lot of factors that affect the incidence of PIP. These are site of injection, size of vein, speed of injection, aqueous phase propofol concentration, and the speed of carrier fluid, propofol temperature, syringe material and drugs used before propofol injection. PIP can be immediate or delayed. Direct irritant effect probably causes immediate pain and kinin cascade activation causes the delayed one.

Lidocaine and opioids are most used pretreatment drugs for prevention of PIP. Lidocaine decreases PIP by inhibiting bradykinin production *via* kinin cascade[16]. Its pH and dilution of propofol in the aqueous phase causes less pain. But sometimes lidocaine fails to decrease pain and can cause some side effects like anaphylactic shock developing immediately after intravenous administration of lidocaine without preservative added to the propofol to decrease injection pain[17].

Opioids such as alfentanil, remifentanil and fentanil are reported to decrease PIP[1,3,11,18]. Opioids effect centrally or peripherally[3]. Opioid receptors are found in the dorsal root ganglia, central terminals of primary afferent nerves and in the periphery[19]. Therefore, the pain reduction effect of opioids on PIP might be on peripheral receptors[20].

Several studies have confirmed effect of opioids on PIP. Basaranoğlu *et al*[18] reported that 1 mcg/kg dose of fentanil and remifentanil are effective in prevention of PIP. Roehm[21] *et al* compared 0.25 mcg/kg/ min remifentanil with 40 mg lidocaine and found that both were equally effective. Nathanson *et al* reported that 1 mg alfentanil and 40 mg lidocaine are effective for prevention of PIP[10]. Lyilikci and colleagues found that alfentanil and remifentanil decreased PIP severity and frequency and also that remifentanil should be used in dose of at least 0.02 mg for this purpose[19]. Kırdemir *et al* concluded that remifentanil 0.5 mcg/kg and alfentanil 1 mg prevent PIP as effectively as lidocaine[22]. Optimum dose of alfentanil in children that reduced PIP was 15 mcg/kg[23]. Fentanyl 100 μg, preceded by one minute venous occlusion was effective in pain reduction during propofol injection in Japanese adults[24]. Cho reported that the combination of cold propofol (4 °C) and pretreatment with 0.5 μg/kg IV remifentanil more effectively decreased the incidence of pain than either treatment alone[25]. Kwak *et al* reported the combination of 0.35 μg/kg/min pretreatment with remifentanil and premixture of lidocaine with propofol was more effective in reducing the incidence of pain on injection of propofol than either treatment alone[26]. Aouad *et al* assessed the combination of two different analgesic modalities (2% 40 mg lidocaine premixed with 180 mg propofol and pretreatment with 2 μg/kg fentanil)[27] and found that both the drugs completely abolished moderate and severe PIP, and significantly reduces the incidence of mild pain when compared with each drug used alone. If all these opioids have a decrement effect on PIP, sufentanil must have the same effect, but at what dosage was our question in this study.

Sufentanil has 10-15 times greater potency than fentanil and 50 times that of alfentanil. It has an immediate onset of action. It is used as an analgesic adjunct in the maintenance of balanced general anesthesia in surgical procedures, for the postoperative management of pain following general surgery, thoracic or orthopedic procedures and cesarean sections *via* epidural route and as an analgesic adjunct to epidural bupivacaine during labor and vaginal deliveries. Its effects on central nervous system, minimal alveolar concentration levels of volatile anesthetics and respiratory depression is similar to the other opioids. Doses more than 2.6 mcg/kg can cause respiratory depression, increase in airway resistance and muscle stiffness after surgery[28]. Its analgesic dose was between 0.01 - 0.03 mcg/kg[29].

Nathanson, Fletcher and İyilikçi *et al*. showed that PIP decreased 30 seconds after alfentanil and remifentanil[10,11,20]. We injected propofol 30 seconds after sufentanil. Sufentanil decreased overall pain incidence from 92.5 to 70%. Sufentanil at 1 mcg dose decreased PIP to 77.5% and at 2mcg dose to 44.5% and this was significant compared to control group. Chung *et al* compared 0.1 mcg/kg, 0.2 mcg/kg, 0.3 mcg/kg sufentanil doses 5 minutes before propofol injection[30]. They reported that 0.3 μg/kg reduced the severity of PIP. Honarmand and Safavi, found that pretreatment with sufentanil 1 mcg did not reduce the incidence and degree of injection pain compared with 0.02 mg remifentanil[31]. However, it decreased pain to 75% compared with saline as we found in our study (77.5%). Low sufentanil dose or the insufficient time period of one minute may have caused this difference. Although we injected propofol 30 seconds after sufentanil, sufentanil decreased overall pain incidence from 92.5 to 70%. Sufentanil at 1 mcg dose decreased PIP to 77.5% and at 2 mcg dose to 44.5% and this was significant when compared to the control group.

CONCLUSION

In conclusion, sufentanil at 1 mcg and 2 mcg doses reduced the incidence and severity of pain on propofol injection. Added to the known advantage of being an adjunct in induction, rapid recovery and lesser need

for postoperative analgesia, sufentanil seems to be an effective alternative to lidocaine for the purpose of reducing the incidence of pain related to intravenous propofol.

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Original Article

Evaluating the Association between Premenstrual Syndrome and Hematologic Parameters during the Early Follicular and Late Luteal Phases

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ABSTRACT

Objective: To determine the relationship between premenstrual syndrome (PMS) and hematologic parameters during early follicular (EF) and late luteal (LL) phases
Design: Cross-sectional study conducted between October 2010 and February 2011
Setting: School of Nursing, Halic University, Istanbul, Turkey
Subjects: One hundred and eighteen healthy young women between 18 and 25 years of age
Intervention: None
Main Outcome Measures: PMS status was evaluated by the Premenstrual Syndrome Scale (PMSS). Biochemical parameters in blood were measured during EF and LL phases.
Results: More than half of the subjects demonstrated PMS (57.6%). Leukocyte and neutrophil counts were found to be elevated during LL phase ($7.24 \pm 1.67 \times 103/mm^3$; $58.84 \pm 8.89\%$) compared with the EF phase ($6.52 \pm 1.42 \times 103/mm^3$; $53.81 \pm 10.76\%$, $p < 0.001$). Class I obese group had higher PMSS scores (143 ± 19.8) than underweight (103.92 ± 23.54) and normal weight groups (122.62 ± 23.54, $p < 0.05$). During the LL phase, subjects with high fasting blood glucose took lower scores (11.8 ± 3.42) from fatigue; those having low iron levels took higher scores from changes in sleeping habits (8.15 ± 2.84) and subjects having normal and low mean corpuscular hemoglobin concentration (MCHC) levels took higher scores (13.67 ± 4.91; 13.64 ± 5.35) from anxiety subscales than others ($p < 0.01$).
Conclusion: Presence of elevated leukocyte value prior to menstruation suggests a relationship between menstrual cycle and inflammation. Class I obese subjects, subjects having low iron, normal fasting blood glucose and low or normal MCHC levels were found to suffer PMS-related symptoms more frequently.

KEY WORDS: menstrual cycle, premenstrual syndrome, women

INTRODUCTION

Women of child-bearing age demonstrate physiological changes on a monthly basis, which are cumulatively called as the menstrual cycle. Ovarian cycle consists of follicular and luteal phases[1]. Premenstrual syndrome (PMS) is a clinical entity which is seen during the late luteal phase of the menstrual cycle (days 21 - 28 of the cycle), recurs during most of the cycles, is alleviated and resolved shortly after the beginning of menstrual hemorrhage, is not observed at least for one week during the follicular phase (days 1 - 4 of the cycle), and presents with physical, emotional, and behavioral changes[2]. The most commonly observed emotional symptoms are increased emotional sensitivity, depression, tension, irritability, anxiety, indecision, attention deficit, forgetfulness, and sleep disorders. Most frequently encountered physical symptoms are breast tenderness, food cravings, acne, edema, pain, and fatigue. Moreover, we can mention social withdrawal, reduced libido, and agitation among the most common behavioral symptoms[3-5]. PMS symptoms can even lead to suicide[6-9].

In Turkey, PMS prevalence has been shown to be 5.9% among women between 15 - 49 years of age and 17.2 - 67.5% among women between 16 - 25 years of age[8,10-14]. Many studies have been conducted about the association between PMS and characteristics of the menstrual cycle among women of childbearing age. However, there are only a few studies focusing on the changes in hematologic parameters occurring before and after the menstruation as well as on the relationship between those changes and PMS. Clancy *et al*[15], found that women with increased hemorrhage

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showed no decrease in erythrocyte and hemoglobin values during the luteal phase[15]. Hunt and Penland[16] found that during the follicular phase, 4% of the women had reduced hemoglobin and 20% had decreased ferritin levels. Blood glucose consumption and carbohydrate oxidation have been shown to be reduced during the early luteal (EL) phase compared with the follicular phase[17]. Varying results have been obtained about the changes in hematologic parameters prior to menstruation (*e.g.*, during the luteal phase) and after the menstruation (*e.g.*, during the follicular phase), and those changes are attributed particularly to the influence of hormones such as estrogen and progesterone[18]. Determining the relationship between hematologic parameters and PMS may contribute to alleviation of the related symptoms. We conducted this study in order to evaluate the association between PMS and hematologic parameters during EF phase and late luteal (LL) phase.

SUBJECTS AND METHOD

Approval of the local ethics committee was taken prior to the beginning of the study. One hundred and eighteen healthy female volunteer students participated. The data were collected by questionnaires and PMS status was evaluated by the Premenstrual Syndrome Scale (PMSS) developed by Gencdogan in 2006[19]. PMSS is a five-point (never: 1 point; rarely: 2 points; sometimes: 3 points; very often: 4 points; always: 5 points) Likert-type scale including 44 items and nine subdimensions. (Appendix 1). PMSS score above 110 points suggests the presence of PMS. There are nine subdimensions of this scale: depressive feeling, anxiety, fatigue, irritability, depressive thoughts, pain, changes in appetite, changes in sleeping habits, and swelling. Cronbach's alpha coefficient is calculated as 0.959 for reliability of PMSS; for subscales the factor alpha ranged from 0.933 and 0.991. We measured fasting blood glucose,

Table 1: Descriptive statistics of the hematologic parameters during the early follicular (EF) and late luteal (LL) phases

Hematologic Parameters		Mean	Standard deviation	Paired t-test	p-value
Fasting blood glucose (70 - 110 mg/dl)	LL	87.04	14.62	1.649	0.102
	EF	84.97	8.43		
Serum Ferritin (11 - 306 ng/ml)	LL	21.56	14.96	1.612	0.110
	EF	19.97	15.15		
Serum Iron (60 - 180 ug/dl)	LL	72.58	37.87	-1.476	0.143
	EF	78.61	39.48		
TIBC (245 - 450 ug/dl)	LL	366.01	63.89	-0.726	0.469
	EF	369.02	56.17		
Leukocyte (4.5 - 10.3 103/mm3)	LL	7.24	1.67	5.207	0.000
	EF	6.52	1.42		
Neutrophil (50 - 70)	LL	58.64	8.89	4.475	0.000
	EF	53.81	10.76		
Lymphocyte (20 - 44)	LL	31.45	8.21	4.733	0.000
	EF	34.97	8.43		
Monocyte(5.1 - 9%)	LL	6.91	2.11	0.936	0.351
	EF	7.12	2.25		
Eozinofil (Eosinophil) (0.9 - 4%)	LL	2.28	1.49	1.375	0.172
	EF	2.12	1.31		
Basofil (Basophil) (0.3 - 1.5%)	LL	0.60	0.39	0.336	0.737
	EF	0.58	0.37		
Erythrocyte (4.38 - 5.77 106/µl)	LL	4.53	0.44	0.858	0.392
	EF	4.50	0.36		
Hemoglobin (13.6 - 17.2 g/dl)	LL	12.87	0.95	0.425	0.672
	EF	12.84	1		
Hematocrit (39.5 - 50.3%)	LL	38.05	2.46	-0.691	0.491
	EF	38.63	2.80		
Thrombocyte (156 - 373 103/µl)	LL	263.67	62.65	-1.501	0.136
	EF	268.48	57.29		
MCH (27.2 - 33.5 pg)	LL	28.66	2.45	0.876	0.383
	EF	28.56	2.38		
MCHC (32.7 - 35.6 g/dl)	LL	33.42	1.27	1.263	0.209
	EF	33.26	1.12		
RDW (11.8 - 13.4 %)	LL	13.72	1.42	0.254	0.800
	EF	13.70	1.57		
MCV (80.7 - 95.5 fl)	LL	85.71	6.12	-1.222	0.224
	EF	86	6.2		

TIBC: Total iron-binding capacity, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, MCV: mean corpuscular volume , RDW: red blood cell distribution width

Appendix 1: Premenstrual Syndrome Scale (PMSS)

There are some descriptive sentences below. Please, read every sentence carefully. After that, mark the scale on the right side of the sentences taking into account the situation in a week before menstruation. Don't evaluate if these situations are experienced at the other times. Please, don't leave a blank for any questions.

A Week Before Menstruation						
		Never	Very little	Sometimes	Frequently	Continually
1	I feel sad					
2	I feel like crying					
3	I am boring					
4	I feel weary					
5	Nothing relish to me					
6	Everything is coming to me					
7	I become pessimistic					
8	I want to take deep breath					
9	I'm afraid such as bad things become at any time					
10	I have increased sensitivity to sounds					
11	I'm afraid such as someone attack from behind me					
12	I feel tired					
13	I think as if everything will be bad					
14	I tire very quickly					
15	I have fears that I can't understand					
16	My heart beats faster than ever					
17	I do not want to deal with anything					
18	Usual works are tiring me					
19	I feel frustrated					
20	I show extreme reaction even to the slightest events					
21	I have difficulty controlling my anger					
22	My relationships are distorted with people around me					
23	My nerves tighten					
24	I feel very anxious					
25	I feel tired more quickly than ever before					
26	I see myself unworthy					
27	I have difficulty of concentrating attention					
28	My attention is distracted easily					
29	I'm lost in thought					
30	I can not think properly					
31	I have headache					
32	My muscles ache					
33	My joints ache					
34	My appetite grows					
35	I want to eat especially farinaceous and sweet foods					
36	I eat more					
37	My sleep desire increases					
38	My sleep has splits					
39	I wake up tired in the morning					
40	I have difficulty falling asleep					
41	My breasts swell					
42	My breasts are very sensitive to the slightest touch					
43	I feel swollen					
44	I do not want to see anyone					

serum ferritin, serum iron, total iron binding capacity, and hemogram values in blood samples obtained during the EF and LL phases. Plasma glucose, serum total iron binding capacity (TIBC) and iron (Fe) was analyzed using the enzymatic kinetic (hexokinase-UV/NAD) method on an Olympus AU400 instrument with Olympus agents. Intra-assay and interassay Co-efficient Variation (CV) percent respectively was for glucose < 3.5%, Fe < 4%, TIBC < 2%. Serum ferritin level was measured by Beckman Coullter (< 10% CV). Hemogram values were analyzed on MH6000 (Medpa) (for Plt CV < 6 for others < 5%). Body Mass Index (BMI) was defined as the body weight (kilograms) divided by height (meters)^2. The categorization of the patients relative to the BMI was carried out according to the classification of the World Health Organization (≤ 18.5, underweight; 18.5 - 24.9, normal; 25 - 29.9, overweight; and 30 - 34.9, Class I obesity)[20]. The individuals with an additional disease (*e.g.*, anemia, ovarian cyst, thyroid disease, etc) were excluded from the study.

Statistical Analysis

The statistical analysis was made with SPSS (Statistical Package for Social Sciences 15.0 version). The data were analyzed by using number and percentage distributions, descriptive statistics (mean, frequency, standard deviation) as well as ANOVA, Tukey, Kruskal-Wallis, Mann-Whitney U tests and Paired t-test.

RESULTS

In this study, the mean age of the subjects was 20.21 ± 2.76 years. The subjects were categorized based on the BMI value as follows: 21.2% were underweight, 69.5% were normal, 7.6% were overweight, and 1.7% were Class I obese. While 57.6% of the study population had a PMSS score ≥ 111 points, 42.4% were found to have a PMSS score < 111 points. The scores of the study sample with regard to the subdimensions of the PMSS are shown in Fig. 1.

Hematologic parameters of the study population during the EF and LL phases are shown in Table 1. No statistically significant difference was found between the measurements performed before and after the menstruation with regard to fasting blood glucose, serum ferritin, serum iron, TIBC , erythrocyte, monocyte, *eosinophil, basophil,* hemoglobin, hematocrit (Hct), thrombocyte, mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular volume (MCV), and red blood cell distribution width (RDW) values ($p > 0.05$). However, leukocyte and neutrophil values during the LL phase were observed to be higher than those during the EF phase, whereas lymphocyte value was found to be higher during the EF phase compared with the LL phase ($p < 0.001$, Table 1). The difference between class 1 obese subjects (PMSS scores:143 ± 19.8) compared to underweight (PMSS scores:103.92 ± 23.54) and normal weight (PMSS scores: 122.62 ± 23.54) subjects is statistically significant ($p < 0.05$).

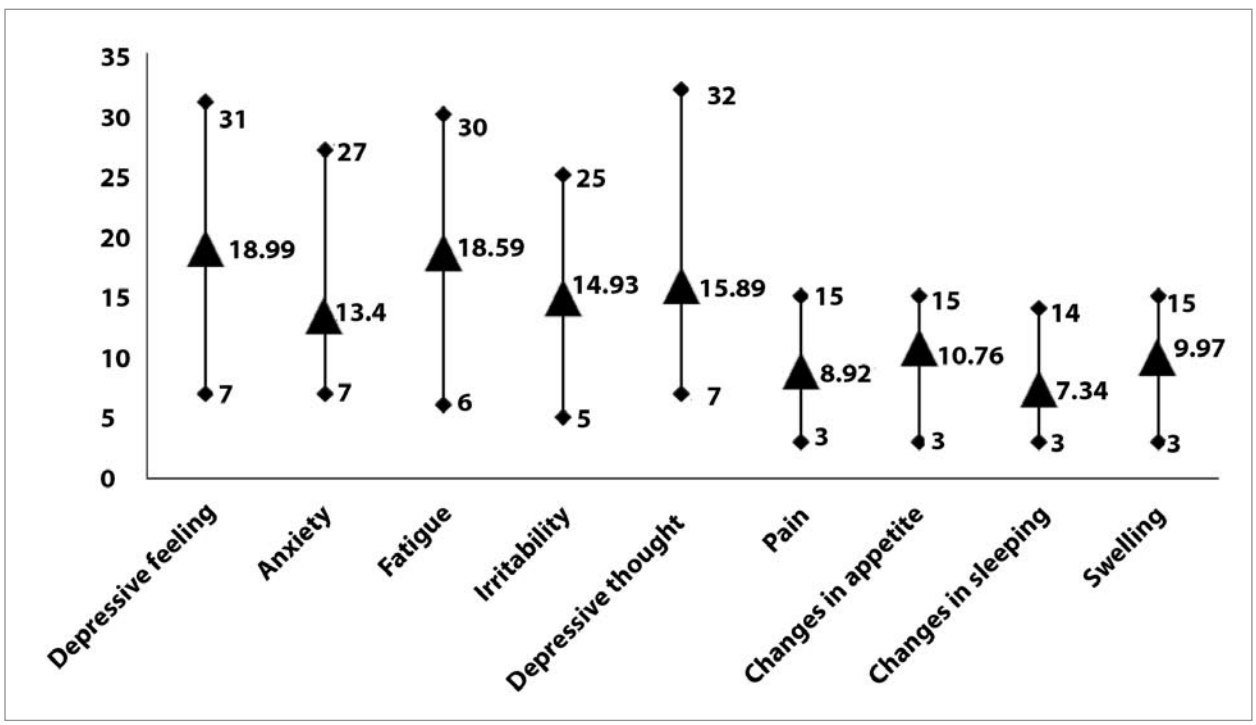

Fig. 1: Descriptive statistics of the premenstrual syndrome scale

Table 2: PMSS results relative to the hematologic parameters during the LL phase

Hematologic parameters during the LL phase	PMS and subscales									
	Depressive feeling	Anxiety	Fatigue	Irritability	Depressive thought	Pain	Changes in appetite	Changes in sleeping habits	Swelling	Total PMS
Fasting blood glucose (70 - 110 mg/dl)										
Low[1]	17 ± 6.56	11.67 ± 5.03	15.67 ± 10.01	13.3 ± 5.51	14.67 ± 10.02	8 ± 5	10.33 ± 1.53	6.33 ± 4.93	8.33 ± 3.51	105.33 ± 48.01
Normal[2]	19.22 ± 6.56	13.62 ± 5.25	18.98 ± 5.29	14.97 ± 4.40	16.17 ± 6	9 ± 3.29	10.78 ± 3.17	7.46 ± 2.87	10.07 ± 3.58	120.28 ± 30.24
High[3]	15.2 ± 5.07	9.6 ± 3.13	11.8 ± 3.42	15 ± 4.74	10.4 ± 4.1	7.6 ± 3.36	10.60 ± 3.36	5.2 ± 3.19	8.8 ± 2.39	94.20 ± 9.26
p-value	0.277	0.146	1 - 2; 0.531 1 - 3; 0.448 2 - 3; 0.005	0.892	0.089	0.603	0.886	0.184	0.454	0.069
KW	2.565	3.844	8.319	0.229	4.837	1.013	0.242	3.391	1.579	5.357
Serum Iron (60 - 180 ug/dl)										
Low[1]	19.19 ± 6.55	13.67 ± 5.35	18.40 ± 5.39	14.44 ± 4	16.08 ± 5.68	8.9 ± 3.52	11.25 ± 3.05	8.15 ± 2.84	10.17 ± 3.55	120.23 ± 29.46
Normal[2]	18.86 ± 6.59	13.28 ± 5.17	18.70 ± 5.68	15.23 ± 4.69	15.83 ± 6.43	8.91 ± 3.22	10.41 ± 3.18	6.80 ± 2.93	9.9 ± 3.55	117.9 ± 31.49
High[3]	19 ± 0	9 ± 0	21 ± 0	18 ± 0	11 ± 0	10 ± 0	12 ± 0	6 ± 0	6 ± 0	112 ± 0
p-value	0.888	0.584	0.873	0.355	0.636	0.953	0.415	1 - 2; 0.020 1 - 3; 0.373 2 - 3; 0.842	0.478	0.875
KW	0.237	1.076	0.273	2.074	0.906	0.096	1.758	5.666	1.475	0.267
MCHC (32.7 - 35.6 g/dl)										
Low[1]	19.19 ± 5.73	13.67 ± 4.91	18.37 ± 5.41	14.11 ± 4.25	16.52 ± 5.96	8.85 ± 3.15	10.26 ± 3.6	7.44 ± 2.98	9.11 ± 3.6	117.52 ± 32.26
Normal[2]	19.33 ± 6.59	13.64 ± 5.35	18.74 ± 5.65	15.39 ± 4.46	15.89 ± 6.17	9.06 ± 3.42	10.94 ± 2.99	7.44 ± 2.96	10.31 ± 3.44	120.74 ± 29.89
High[3]	13.33 ± 7.34	8.83 ± 1.83	17.5 ± 4.76	12.17 ± 3.13	13 ± 5.83	7.17 ± 2.32	10.5 ± 3.02	5.33 ± 2.25	9.17 ± 4.49	97 ± 25.1
p-value	0.145	1 - 2; 0.843 1 - 3; 0.024 2 - 3; 0.015	0.843	0.121	0.457	0.295	0.755	0.231	0.298	0.163
KW	3.865	6.080	0.341	4.224	1.564	2.439	0.562	2.933	2.422	3.632
Neutrophil (50 - 70%)										
Low[0]	16.94 ± 5.47	11.75 ± 4.85	16.25 ± 5.14	13.94 ± 4.19	14.06 ± 5.30	8.13 ± 2.96	10.88 ± 2.83	6 ± 2.25	9.31 ± 3.88	107.25 ± 23.96
Normal[1]	18.81 ± 6.82	13.14 ± 5.10	18.5 ± 5.6	14.82 ± 4.6	15.75 ± 6.22	8.8 ± 3.4	10.68 ± 3.19	7.44 ± 3.05	9.98 ± 3.48	117.91 ± 31.57
High[2]	22.5 ± 4.2	16.93 ± 5.14	21.86 ±3.98	16.79 ± 2.89	18.86 ± 5.48	10.57 ± 2.79	11.14 ± 3.23	8.21 ± 2.67	10.71 ± 3.6	137.57 ± 21.45
p-value	0.056	0 - 1; 0.575 0 - 2; 0.017 1 - 2; 0.028	0 - 1; 0.277 0 - 2; 0.014 1 - 2; 0.081	0.189	0.090	0.104	0.869	0.097	0.561	0 - 1; 0.386 0 - 2; 0.017 1 - 2; 0.059
F value	2.952	4.351	4.107	1.693	2.459	2.307	0.141	2.378	0.582	4.051

KW: Kruskal Wallis test, t: İndependent-Samples t-test, F: ANOVA Tukey, LL: Late Luteal, PMSS: Premenstrual Syndrome Scale, MCHC: mean corpuscular hemoglobin

Depressive feeling subscale scores of the underweight patients (15.24 ± 5.7) were lower than those of the normal weight patients (20 ± 6.37, $p < 0.001$). Depressive thought subscale scores were observed to be lower in underweight subjects (13.36 ± 5.27) than in normal weight (16.44 ± 6.17) and Class 1 obesity subjects (24 ± 1.41), whereas overweight subjects were found to show lower depressive thought subscale scores (16.11 ± 5.97) than Class 1 obese subjects ($p < 0.05$). Swelling scores were lower in underweight subjects (8.4 ± 3.29) than in normal weight (10.41 ± 3.52) and overweight subjects (11.11 ± 3.02, $p < 0.05$).

The comparison of PMSS scores with TIBC, serum ferritin, leukocyte, *eosinophil*, *basophil*, monocyte, erythrocyte, hemoglobin, hematocrit, thrombocyte, MCH, RDW, and MCV values during the LL phase, revealed no statistically significant difference ($p > 0.05$, Table 1).

The subjects with an elevated fasting blood glucose level during the LL phase were found to display lower fatigue scores compared with the individuals with a normal fasting glucose value during the same phase ($p < 0.01$). The subjects with a normal serum iron level were found to exhibit lower anxiety scores than those with reduced serum iron levels ($p < 0.05$). The subjects with a raised MCHC level were observed to demonstrate lower anxiety scores compared with the subjects showing normal or lower MCHC levels, whereas the subjects with an increased neutrophil count were determined to exhibit higher anxiety scores compared with the subjects with a low or normal neutrophil level. Also, they were observed to demonstrate higher fatigue and total scores compared with the subjects with low neutrophil count ($p < 0.05$, Table 2).

DISCUSSION

In the current study, leukocyte and neutrophil levels were elevated during the LL phase compared with the EF phase, whereas lymphocyte values demonstrated an increase during the EF phase. Reproductive mechanisms such as menstruation, ovulation, and implantation are believed to trigger the inflammation process. Endometrium undergoes a regeneration during each menstrual cycle. This regeneration process involves the differentiation of a new lining in place of the existing functional layer in order to allow the implantation of the embryo. Mediators involved in the inflammatory response such as cytokines, chemokines, and prostanoids, have been shown to be activated throughout the menstrual cycle in synch with the accumulation of leukocytes in the endometrium[21]. Both estrogen and progesterone have been shown to bear potential proinflammatory and anti-inflammatory effects. The elevated leukocyte count in the endometrium during the late secretory phase is followed by a decline in progesterone concentration[22]. Salamonsen and Wooley showed raised neutrophil counts as well as elevated lymphocyte levels in the endometrium during the 26th and 28th days of the menstrual cycle compared with the values before the menstruation[23]. Lymphocytes continue to be active throughout the proliferative phase of the uterus, however, this activity shows a decrease during the secretory phase which is thought to be associated with progesterone[24]. No significant difference was observed in fasting blood glucose levels before and after the menstruation. The changes occurring in estrogen and progesterone concentrations throughout the follicular and luteal phases are thought to cause a difference between the phases with regard to energy consumption[25,26]. Glucose consumption and carbohydrate oxidation have been shown to decrease during the early luteal phase compared with the follicular phase[27]. In this study, 57.6% of the study population were determined to have PMS according to the PMSS. Tanriverdi *et al* found the prevalence of PMS in their study as 67.5%[28]. When the scores of the subdimensions were evaluated: anxiety, depressive thoughts, and changes in sleeping habits demonstrated no significant change, whereas depressive feeling, fatigue, irritability, pain, changes in appetite, and swelling exhibited significant changes.

In the current study, underweight women were observed to experience no PMS, whereas normal weight and overweight women were found to suffer from PMS. In addition, scores of depressive feeling, depressive thoughts, and swelling subdimensions were also determined to have a positive correlation with BMI. Bertone-Johnson *et al* found that there was a strong relationship between BMI and PMS, while they associated raised BMI with many physical and emotional symptoms such as swelling in extremities, back pain, abdominal cramps, diarrhea, emotional fluctuations, and increased appetite[29]. Women experience a desire to eat more frequently and choose foods with rich fat or energy content during the luteal phase of the menstrual cycle compared with the follicular phase; this has been shown to be due to increased energy consumption during this period[30]. The changes involving regulation of appetite are also known to be associated with the homeostasis of the fasting blood glucose. Although studies in this field produce contradictory results, it is reported that insulin response is regulated by sex hormones and insulin sensitivity is lower during the luteal phase compared with the follicular phase[31-32]. In this study, women with elevated fasting blood glucose levels were found to have lower fatigue scores compared with those with a reduced fasting blood glucose value. Elevated fasting glucose levels were observed to be

close to the normal values. Estrogen has an influence over plasma fasting blood glucose levels and this may lead to different responses against hypoglycemia. Glucose levels have been shown to be lower during the luteal phase compared with the follicular phase[33]. Decreased glucose levels and an increased appetite for sweets during the luteal phase may indicate the metabolic need for sugar. This may be the reason why people with elevated sugar levels are affected less by fatigue.

The women with low iron levels were found to have higher scores for changes in sleeping habits compared with the ones with high iron levels. Pittori *et al* found that having low values for anemia-related parameters (serum ferritin, complete blood count) caused excessive weakness, fatigue, sleep disorders, headache, anxiety, hair loss, and nail breakage[34]. As a result of impaired monoamine oxidase activity, iron deficiency is associated with apathy, drowsiness, irritability, reduced attention and concentration, and memory loss[35]. The individuals with a normal or low MCHC levels were found to have higher anxiety levels compared with those with high MCHC values. Maes *et al* found that examination stress significantly reduced hemoglobin, hematocrit, MCV, MCH, and MCHC levels[36]. In this study, the individuals with higher neutrophil levels were observed to experience anxiety, fatigue, and PMS more frequently compared with the ones with normal and high neutrophil values. Stress, anxiety or negative emotions were thought to affect hematologic parameters in a negative way. The stress-related changes in hematologic parameters were observed to be more frequent among people experiencing stress-related anxiety. This suggests that personality traits may be influential in stress-related hematologic responses.

CONCLUSION

Our study shows that women with low serum iron levels, low and normal MCHC, and normal fasting blood glucose, as well as those with elevated BMI experience the symptoms of PMS more frequently.

Women with a high neutrophil count during the LL phase suffer PMS more frequently, as well. The raised values of leukocyte count prior to the menstruation suggest that menstrual cycle is associated with inflammation. Moreover, menstrual cycle is thought to be a serious source of stress for young women. Our study reveals the importance of controlling BMI, anemia, and blood sugar with regard to alleviation of PMS symptoms.

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Case Report

Hypertension and Hypoglycemia in a Child with Hepatoblastoma: A Case Report

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ABSTRACT

Hepatoblastoma is the most common malignant tumor in the pediatric age group. It is treated with chemotherapy and surgery with excellent results. In majority of the cases ,the course of treatment is uncomplicated. Rarely there could be unexpected complications like hypertension due to hypersecretion of renin or severe hypoglycemia due to production of insulin like substances by tumor cells. These episodes can complicate the management of the case. We report a rare case of hepatoblastoma in an eight-year-old child who had both the complications. To the best of our knowledge, this is the first such case to be reported in literature.

KEY WORDS: chemotherapy, hepatoblastoma, hypertension, hypoglycemia

INTRODUCTION

Hepatoblastoma is a rare aggressive childhood tumor accounting for 75% of primary liver tumors in the pediatric age group. The five-year survival has increased to nearly 70%[1, 2] with the use of cisplatin-based chemotherapy and advanced surgical techniques. Paraneoplastic syndromes which can cause metabolic complications are rarely reported. We present the case of a hepatoblastoma patient who had hypertension, hypoglycemia, hypokalemia, hyonatremia and hypomagnesemia. In hepatoblastoma, there are anecdotal case reports of hypertension due to hyperreninemia[3] or hypoglycemia due to hyperinsulinemia[4], but to the best of our knowledge, this is the first case that had so many complications at the same time.

CASE REPORT

An eight-year-old Indian boy presented with right upper abdominal pain. On examination there was hepatomagaly and ascites. Computerized tomography (CT scan) revealed multiple hypoechoic lesions in both lobes of the liver, the largest measuring 4 x 4.5 cm, with some lesions showing calcification (Fig. 1). The ascitic fluid was hemorrhagic but negative for malignant cells. The alfafetoprotein (AFP) was 1,231,760 IU/ml. Needle biopsy confirmed epithelial (fetal subtype) hepatoblastoma (Fig. 2). The CT- scan of the chest was negative for pulmonary metastasis. He was started on SIOPEL 3 high risk protocol and he tolerated the first course well. During the 2nd course of chemotherapy, he had hypertensive encephalopathy with seizures. EEG, CSF study, CT brain were normal. Renal artery Doppler study was also normal. Plasma renin was 12 pmol/l (normal range 0.264 – 2.4 pmol/l) with normal plasma aldosterone level. After few days, he had unexplained recurrent hypoglycemic episodes. Plasma insulin level was 0.2 uU/ml (normal range 2.6 – 24.9) and insulin like growth factor – I (IGF-1) was < 5 nmol/l (range 10 – 66 for P1 Tanner stage). He also had persistent asymptomatic hyponatremia (Serum Na+ < 120 mmol/l), mild hypokalemia, and hypomagnesemia. His hypertension, hypoglycemia, and electrolytes were treated appropriately. He was continued on chemotherapy with weekly AFP monitoring. Unfortunately after three cycles of chemotherapy (day 29), AFP was rising (1,716,390 IU/ml) and US abdomen showed no response with increasing ascites. His parents took him to his native country where he died.

DISCUSSION

In the literature, only few cases were reported with hyperreninemia in non-renal non-hepatic malignant tumors[5,6], and non-malignant liver tumors[7]. In the case reported by Moritake *et al*[3], a hepatoblastoma child had hypertension at presentation due to hyperreninemia. The child had neoadjuvant chemotherapy, tumor resection, and postoperative chemotherapy. Renin secretion in the tumor specimen was documented. In our case, due to various logistical reasons, tumor analysis for renin secretion could not be documented.

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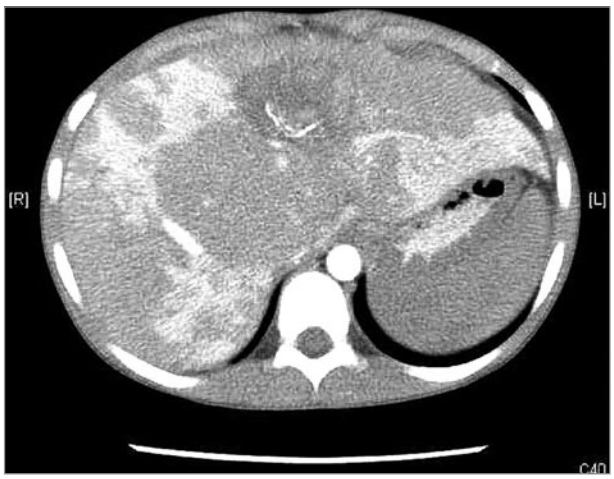

Fig. 1: Axial CT scan of the abdomen showing multiple hypodense hepatic lesions involving both liver lobes.

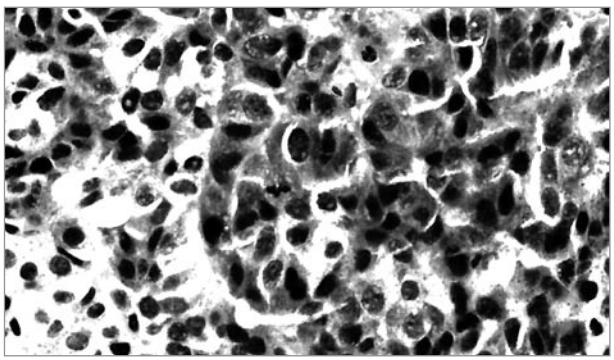

Fig. 2: H & E (x 400) Trabecule of cuboidal and polygonal malignant cells with eosinophilic cytoplasm and moderate mitosis mimicking hepatocytes.

Moritake *et al*[3] reported drop in plasma renin activity after surgery and chemotherapy, but our patient did not respond to chemotherapy, hence did not undergo surgery. Literature analysis showed curative resection as the only definitive method of bringing down the plasma renin activity[5-7].

The second serious episode in our patient was attack of severe hypoglycemia. Ha *et al*[4] reported a case of hepatoblastoma in a 5-year-old boy who developed hypoglycemia and they documented low endogenous insulin and increased insulin-like activity (ILA) in the serum and tissue specimen and abnormalities for carbohydrate metabolism. In their case, the child presented with an episode of severe hypoglycemia while our patient developed hypoglycemia only during the administration of the second cycle of chemotherapy. This condition was described as non-islet-cell tumor hypoglycemia (NICTH) or hypoinsulinemic hypoglycemia related to high levels of high molecular weight IGF–II[8,9], also referred to as "Big IGF-2". Unfortunately, our lab did not have the facility to measure this type of IGF-2. Hijuka *et al*[9] reported a series of 44 adult patients in which presence of serum IGF-II due to non-islets tumor led to hypoglycemia. But this condition was reported in a series of elderly patients with hepatocellular carcinoma or gastric carcinoma. No case report or series has been published in recent time in pediatric patients describing this complication. de Groot *et al*[10] described this phenomenon as over-expression of the IGF-II gene by tumor. The only treatment described in the literature for this complication is surgical removal of the tumor. Unfortunately our patient could not undergo any surgery due to poor response to chemotherapy and poor performance status. Presence of hypokalemia was also described by authors[6], which was also present in our case. However, the severe hyponatremia and hypomagnesemia seen in this case was not described earlier..

CONCLUSIONS

We report this case to highlight the paraneoplastic manifestations of hepatoblastoma like hyperreninemia and the presence of insulin-like growth factor substances. To the best of our knowledge, there is no reported case of hepatoblastoma which had both hyperreninemia and severe hypoglycemia with electrolyte abnormalities.

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Case Report

Spinal Cord Demyelination in Biotinidase Deficiency: A Case Report

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ABSTRACT

Biotinidase deficiency is a treatable cause of severe neurological disorders and skin disorders. Most symptomatic patients will have neurological, cutaneous manifestations and typical organic aciduria. Spinal cord involvement is a rare manifestation of this disease and is commonly unrecognized. We report a previously healthy boy who presented at the age of 28 months with recurrent ataxia and mild alopecia, and MRI evidence of spinal cord demyelination. Biotinidase deficiency was confirmed later. Supplementation with biotin resulted in disappearance of the symptoms and normalization of the MRI spinal cord changes. Biotinidase deficiency, as a treatable condition, should be considered in the differential diagnosis in any child who presents with neurological symptoms and spinal cord demyelination with or without alopecia.

KEY WORDS: alopecia, ataxia, biotinidase deficiency, myelopathy

INTRODUCTION

Biotinidase deficiency is an autosomal recessive inherited disorder with worldwide estimated incidence of 1:80,000-1:100,000[1-2]. It can be either profound with biotinidase activity being less than 10% of mean normal activity or partial with 10 to 30% of mean normal activity[2-5].

Most patients usually present with neurological abnormalities, with refractory seizures being the most common problem. Other symptoms include hypotonia, ataxia, sensorineural deafness, optic atrophy, developmental delay, metabolic acidosis and stridor[1,6]. Cutaneous features include seborrhoeic and atopic dermatitis and partial or complete alopecia[1], but they are not always present. Other clinical manifestations include kerato-conjuctivitis, glossitis and fungal infection[7]. The patient with partial biotinidase deficiency may be healthy and develop symptoms only when stressed by infection or starvation.

We report a case of biotinidase deficiency with atypical clinical presentation and unusual spinal cord involvement.

CASE REPORT

A 28-month-old boy was admitted because of recurrent ataxia. He had three episodes within eight weeks before seeking medical advice. He was reported to be normal between attacks but later his symptoms became persistent. These attacks were precipitated by intercurrent infection, and were also associated with history of hair loss.

His perinatal history was unremarkable as he had normal development milestones. He was born to 1st degree cousin Syrian parents and had two brothers who were healthy at the time of his presentation. Clinical examination showed an afebrile child with angular stomatitis and mild alopecia. Vital signs including respiratory rate, blood pressure were all normal. His cranial nerves, limb power and deep tendon reflexes were also normal. Tone was increased around both ankles, was normal in the upper limbs, sensation was intact and he had an ataxic gait with Romberg sign negative.

His cardiovascular, respiratory and abdominal examinations were normal and there was no incontinence. Laboratory investigation showed a normal complete hemogram, serum electrolyte, liver and renal profile. Serum lactic acid done three times, was high once: 5.12, 0.94, and 2.3 (normal = 0.5 – 2.2 mmol/l). Serum ammonia was 63 (normal: 11 – 60 mmol/l). Urine showed no ketones. Blood for amino-acid chromatography and urine for organic acid chromatography were normal.

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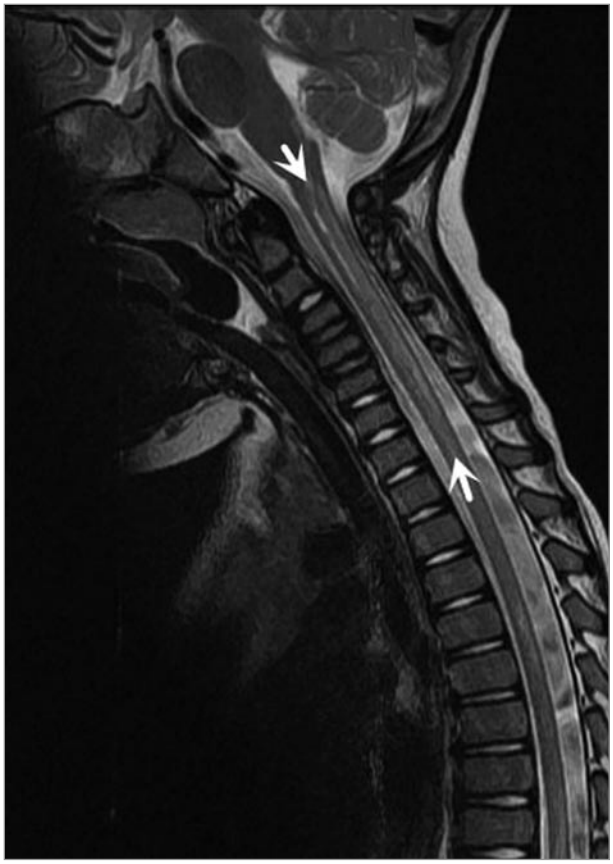

Fig. 1: MRI T2 weighted image showing the abnormally increased signal intensity within the cervical segment of the spinal cord (between arrows)

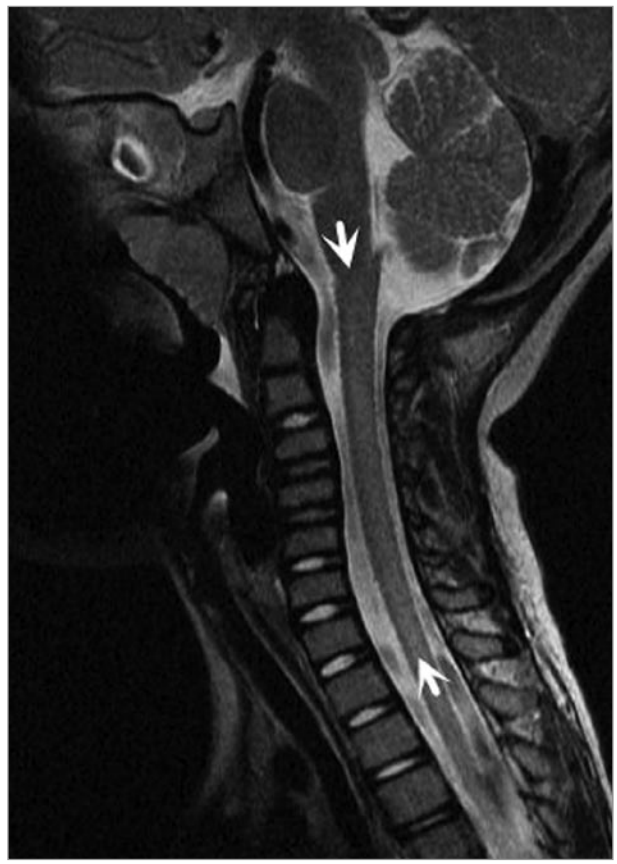

Fig. 2: Normal follow-up MRI of same cervical segment (between arrows)

The cerebrospinal fluid (CSF) lactic acid was found to be raised on two occasions: 6.55 and 5.11 (normal = 0.5 – 2.2 mmol/l). Cell count, glucose, protein all were within normal range. Brain computerized tomography (CT), magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) were all normal. MRI spine showed evidence of swollen cord with hypo-intense signal in T1, hyper-intense in T2 from cervical region down to dorsal D2 – D3. This showed subtle enhancement with contrast suggestive of possible infiltrative lesion (*e.g.*, astrocytoma) or demyelination (Fig. 1, 2). Neurophysiology studies like EMG, NCV were not done.

Abnormal tumor cells were excluded by CSF cytology. He received steroids for seven days for the possibility of inflammatory demyelinating lesion. By this time the serum biotinidase activity result came back as low, *i.e.*, = 2.7 unit (normal 4.4 – 12 unit) which is diagnostic of biotinidase deficiency. Steroid was tapered, and he was started on biotin with a dose of 10 mg daily.

During his follow-up he showed progressive improvement in gait and hair, with complete normal neurological examination except for non-paralytic squint. This was seen only during his recovery from the illness and this was not associated with visual or hearing problems. Follow-up MRI spine showed mild improvement after four months with complete resolution after 16 months of treatment.

It is worth mentioning that his younger brother came later with ataxia at age of three years. This was not associated with alopecia or skin rash and clinically no weakness. MRI brain was not done because of the previously affected sibling. His biotinidase assay was checked immediately and it was confirmed that he was also similarly affected. He was started on biotin supplementation. His clinical signs were less than that in the index case, possibly related to early presentation because of early recognition of symptoms by the parents.

DISCUSSION

Biotin is a co-factor for five carboxylase enzymes involved in gluconeogenesis, aminoacid catabolism and fatty acid synthesis (pyruvate carboxylase, propionyl-CoA carboxylase, 3-methyl-crotonyl-CoA carboxylase and two isoenzyme of acetyl-CoA carboxylase).

When there is a defect in biotin metabolism there will be deficiency in all of the carboxylases, hence multiple carboxylase deficiency[1].

Table 1: Biotinidase deficiency myopathy or spinal cord lesion[7,12,13]

	Index patient	Ref[12]	Ref[13]	Case 1[7]	Case 2[7]
Clinical presentation					
Age of onset	26 months	18 months	36 months	7 ½ yrs	5 yrs
Ataxia	+	+	+	-	+
Dysathria	-	+	NA	-	NA
Seizure	-	-	-	-	-
Skin rash	+	+	-	+	+
Alopecia	+	+	+	-	+
Weakness	+	-	+	+	+
Laboratory Findings					
Abnormal urine for organic acids	-	+	+	+	+
Lactic acidosis	+	-	+	+	+
S. Ammonia	Normal	NA	Elevated	NA	Normal
MRI Spinal cord	Abnormal signal of spinal cord white matter	Abnormal signal of spinal cord white matter	Abnormal signal of spinal cord white matter	Abnormal signal of spinal cord white matter	Abnormal signal of spinal cord white matter
Nerve conduction, EMG	ND	N	NA	Abnormal(↓ motor conduction velocity)	NA

+: present, -: absent, NA: not available, ND: not done, NCV: nerve conduction velocity, ↓: decreased

Biochemical finding are variable and often reveal hyperammonemia, raised lactic acid concentrations in blood or cerebrospinal fluid and abnormal urinary organic acid excretion, especially, increase in 3-hydroxyisovaleric acid, B-methylcrontonylglycine, B-hydroxypropionate and methyl citrate.

There are two enzyme deficiencies that cause multiple carboxylase deficiencies. The one is biotinidase which is responsible for recycling of endogenous biotin[1,8] and the other is holocarboxylase synthetase deficiency which prevents the attachment of biotin to apocarboxylase[1,9].

The disease can be diagnosed by a flourimetric or colorimetric enzyme assay in serum. The locus of the biotinidase gene has been mapped to chromosome 3 in band p25. First trimester prenatal diagnosis for biotinidase deficiency has also been performed[10].

Neurological dysfunction in children with biotinidase deficiency manifests in the first few years of life and typically presents with seizures, ataxia that is associated with, skin rash and alopecia[11]. Children with delayed clinical onset have optic atrophy, spastic paraparesis and electromyographic evidence of neuropathy as their presenting feature[11]. Our patient had onset at 28 months. He had features seen in children with early onset biotinidase deficiency but they were mild including episodic ataxia, mild alopecia and minimal skin lesion. Unlike many of those with early onset, he had normal brain CT and MRI. Furthermore, he had evidence of myelopathy on MRI spinal cord, a finding rarely reported in children with onset after five years[11]. Spinal cord involvement is rare in biotinidase deficiency and is often difficult to recognize. In 1992, Honavar *et al*[7,11] reported a patient with biotinidase deficiency and a progressive neurological disorder who died just before the biochemical diagnosis was established. Postmortem examination of the brain, and spinal cord revealed necrotizing lesions similar to those seen in Leigh's disease and Wernicke encephalopathy. In addition, there was severe focal edema in deep cerebral grey matter, brainstem and spinal cord[7,11]. In our patient, MRI T2 weighted sequence revealed an extensive hyper-intense lesion involving the cervical spinal cord down to the dorsal segment with inflammatory myelitis as a possibility; this suggest that the differential diagnosis of unexplained spinal cord demyelination should include biotinidase deficiency.

Dermatological lesions are a major feature of biotinidase deficiency[7]. Our patient had mild perioral lesions and mild alopecia. These could be mistaken for nutritional problems. However, after treatment with biotin dramatic improvement was observed.

Several studies have described patients with spinal cord involvement in biotinidase difficiency. Table 1 compares such patients with our patient[7,12,13].

Treatment with oral biotin (5 - 20 mg/day) is both cheap and rewarding especially if started early. The clinical symptoms, neurological and neurophysiological findings as well as biochemical findings will normalize after biotin therapy, whereas delay in treatment leads to severe intellectual, neurological, visual and hearing impairment.

CONCLUSION

In our culture, with high rates of consanguineous marriages, one should always suspect inherited metabolic disease. Biotinidase deficiency is one of them. The disease is variable in its clinical, laboratory, and

radiological features. Early diagnosis and recognition and hence treatment with biotin are essential to prevent permanent neurological disability. This may strengthen the argument for universal neonatal screening particularly in societies like ours with high rate of inter-marriages.

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Case Report

Gaucher Disease Co-existing with Wilson Disease: A Case Report

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ABSTRACT

A ten-years-old girl diagnosed as a case of Gaucher disease with co-existent Wilson disease developed Wilsonian fulminant hepatic failure as pre-terminal illness. The association of Gaucher diaease and Wilson's disease in same child has not been described before.

KEY WORDS: autosomal recessive disorder, hepatosplenomegaly, metabolic disorders

INTRODUCTION

Gaucher disease (GD) is an autosomal recessive metabolic disorder. It occurs due to deficient acid β-glucosidase activity. Among the three types of the disease type 1 Gaucher is most common variety which usually presents with hepatosplenomegaly and pancytopenia. Wilson disease (WD) is also an autosomal recessive disorder. Absence or malfunction of the gene ATP7B localized to chromosome 13 (13q14.3) is responsible for abnormal copper metabolism in this disorder[1-3]. We report a case of GD in a ten year old girl who subsequently was diagnosed with WD and fulminant hepatic failure.

CASE REPORT

A ten-year-old female child was referred to our institute with history of fever and pallor for last four months. Referral diagnosis was pancytopenia. The child had anemia and hepatosplenomegaly at admission without any associated bone pain or bleeding diathesis. Other systems were within normal limits. There was nothing significant in birth history. Development was as expected. She was immunized according to national schedule.

The child was investigated extensively, which showed hemoglobin of 7.2 gm / dl and total leucocyte count of 2300 / mm^3. The differential count was 38% polymorphs, 57% lymphocytes, 2% eosinophils and 3% monocytes. Her platelet count was grossly reduced. Her chest X-ray, Mantoux test, urine and stool analysis were non-contributory. Her metabolic profile showed sodium 136 meq/l, potassium 2.9 meq/l, blood urea 15mg/dl, serum creatinine 0.6 mg/dl, total serum bilirubin 1.2 mg/dl, aspertate transaminase 30 IU/l, alanine transaminase 91 IU/l, serum albumin 3.2 gm/dl, globulin 3.0 gm/dl and alkaline phosphatase was 524 IU/l. Sonography of abdomen showed huge splenomegaly, thick walled gall bladder but there was no evidence of portal hypertension. Upper gastro intestinal (GI) endoscopy was within normal limit. Her serum hepatitis B surface antigen, anti nuclear factor and double stranded DNA were negative. Aldehyde test was negative but direct agglutination test (DAT) for leishmaniasis was weakly positive. Bone marrow biopsy showed erythroid hyperplasia with some foamy cells. Enzymatic study was done to rule out lipid storage disease. It showed normal sphingomyelinase activity but β-glucosidase activity was grossly deficient < 1.00 nmol/hr/mg (normal > 5.00 nmol/hr/mg).

Anti-leishmania therapy was started, initially, in view of clinical suspicion and mildly raised DAT for leishmaniasis but it was stopped when enzyme study revealed abnormally low β-glucosidase activity confirming GD. She was diagnosed as a case of adult type non-neuropathic GD (Type I) at discharge during first admission.

The child was followed up in our outpatient department. She developed jaundice after two months with persistence of hepatosplenomegaly. She was again investigated to complete the work up; which showed antibody against hepatitis C virus, liver- kidney microsomal antibody (LKM) and anti-smooth muscle antibody were negative. Work up for WD showed presence of Kayser-Fleischer (KF) ring, low serum

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ceruloplasmin 12.7 mg/dl {normal (> 20) mg/dl}, and pre-penicillamine urinary copper excretion of 990.60 ug/l (normal < 30 ug/l). Post penicillamine urinary copper excretion study was not done. The child was given supportive management, antibiotics and D-penicillamine therapy.

Over next two months, she gradually developed progressive liver failure. Ultimately, she required to be admitted again with hepatic encephalopathy and fulminant hepatic failure. Further investigations during last admission showed hemoglobin of 7.6 gm/dl, total leucocyte count of 11,900/mm^3 with differential count of 53% polymorphs, 44% lymphocytes and platelet count of 80,000/mm^3. Her metabolic profile showed serum hyponatremia (sodium 121 meq/l), hypokalemia (potassium 2.2 meq/l), blood sugar 77 mg/dl, blood urea 52 mg/dl, serum creatinine 0.9 mg/dl, total serum bilirubin 7.3 mg/dl with conjugated fraction 4.9 mg/dl, aspertate transaminase 21IU/l, alanine transaminase 13IU/l, serum albumin 2.3 gm/dl, globulin 4.0 gm/dl, alkaline phosphatase 94IU. Her international normalized ratio (INR) for prothrombin time (PT) was 3.95 activated partial thromboplastin time (APTT) was 52 sec (normal 25 sec). Her repeat ultra sonogram of abdomen revealed coarse hepatic echo texture with features of portal hypertension with ascites. Ascitic fluid analysis was suggestive of peritonitis with total cell count of 1650/mm^3 with 50% polymorphs, sugar 86 mg/dl and protein 2.8 gm/dl but culture was negative. She succumbed to her illness five days after admission in spite of standard management for fulminant hepatic failure and its associated complication.

DISCUSSION

GD, an autosomal recessive metabolic disorder occurs due to deficient acid β-glucosidase activity[1]. There are three clinical subtypes delineated by presence and progress of neurological manifestations: Type 1 or the adult, non-neuronopathic form; type 2, the infantile or acute neuronopathic form, and type 3 the juvenile or Norrbottnian form. Among all the forms, type 1 is most common and accounts for 99% of cases[2,3].

WD is an autosomal recessive disorder of abnormal copper metabolism. It results from absence or malfunction of ATP7B gene localized to chromosome 13 (13q14.3)[4]. It is known to have varied hepatic presentation, ranging from asymptomatic state to chronic hepatitis and fulminant hepatic failure[3].

Type 1 GD usually present with hepato-splenomegaly and pancytopenia without any neurological manifestations. Hepatic inflammation usually does not occur in case of Gaucher disease. Only rare instances of chronic active hepatitis[4] and fulminant hepatic failure have been reported in adults[5]. Rarely the disease may be associated with pulmonary hypertension, exopthalmos[6] or growth hormone deficiency[7].

In our case, the initial clinical presentation was hepatosplenomegaly and pancytopenia consistent with storage disease. Nieman-Pick Disease was excluded by normal sphyngomyelinase level. Reduced glucosidase activity confirmed the diagnosis of GD. But, the progressive and relentless deterioration of hepato-cellular function over two months was highly unlikely. She was further investigated which revealed co-existent WD. In all likelihood, she succumbed to Wilsonian liver failure[8].

To the best of our knowledge, co-existence of GD and WD has not been reported before.

CONCLUSION

Our case had simultaneous existence of two autosomal recessive metabolic disorders, namely, GD and WD. She developed fulminant hepatic failure as her pre-terminal illness. Though it is rare, two metabolic disorders like GD and WD may be present in a same patient.

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Case Report

Neonatal Cardiac Tamponade: What is the Cause?

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ABSTRACT

We present one case of neonatal cardiac tamponade due to percutaneous jugular venous catheterization, a rare and potentially fatal complication. In neonates with central venous catheters, the incidence of pericardial effusion (PCE) with tamponade is 0.5 - 2%. Perforation usually has a delayed course and results from endothelial injury, caused by the fluids, which leads to necrosis and thrombosis. This fluid then diffuses transmurally across the myocardium into the pericardium. Even if the catheter tip is placed properly and checked immediately after placement, it can migrate, an incidence which implies that the position of the catheter be checked at least twice a week after insertion.

KEY WORDS: myocardium, newborn, ventilation

INTRODUCTION

Central venous catheterization is frequently used in infants in the neonatal intensive care setting and is associated with several complications, including occlusion, infection, thrombosis, breakage, displacement and migration of the catheter plus perforation of the vessel wall[1]. We present a case of neonatal cardiac tamponade due to percutaneous jugular venous catheterization, a rare and potentially fatal complication.

CASE REPORT

A 27-week preterm male baby born by normal vaginal delivery with a birth weight of 1.080 kg was admitted immediately and ventilated after birth in Al-Sabah Maternity NICU with a diagnosis of hyaline membrane disease.

The baby received two doses of surfactant and was on high frequency oscillatory ventilation since 10 hrs of age. He improved gradually and was extubated after eight days. Feeds were started and gradually increased while the baby was shifted to special care unit to continue his care.

At 51 days of age, a percutaneous central catheter was electively inserted through the left external jugular vein and placed at the root of the superior vena cava. The position was confirmed by chest X–ray. Intravenous fluids were started through this route. The baby remained stable for six days initially and then he had sudden desaturation and bradycardia for which he was shifted back to the NICU, intubated and was put on mechanical ventilation.

His BP was 76/49 mmHg, MAP 35 mmHg and HR was 157 bpm. A chest X-ray taken at this stage showed cardiomegaly and there was migration of the catheter tip from superior vena cava to the right ventricle. Echocardiography (ECHO) confirmed significant pericardial effusion with tamponade. Intravenous fluids were immediately stopped and the percutaneous jugular catheter was removed. The pericardial effusion was drained immediately by ECHO guided subxiphoid pericardiocentesis. Approximately 32 ml of clear fluid was aspirated from the sac. Biochemical analysis of this fluid proved it to be the infusate. ECHO done 12 hrs later, showed complete clearing of the fluid.

The baby improved after this and was extubated and later discharged in a satisfactory condition.

DISCUSSION

Pericardial effusion (PCE) with tamponade is a rare complication of central venous catheters associated with high mortality[1]. In neonates with central venous catheters, the incidence of PCE with tamponade is 0.5 - 2%, and mortality varies from 45 to 67%[2].

A study by Beardsall *et al* estimated the frequency of PCE with cardiac tamponade occurring with percutaneous long lines to be 1.8 / 1000 lines[3]. High fatality is due to its sudden onset and fast deterioration.

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Timely diagnosis and drainage has been proven to be life-saving. In the Beardsall study the median time from CV line insertion to presentation was three days (range of 0 - 37 days), with nearly two-third cases presenting as sudden cardiovascular collapse, and most of the rest having unexplained cardiorespiratory instability[3]. In our case, the interval between line insertion and the clinical deterioration was six days.

Myocardial perforation and effusion can either occur at the time of cannulation or later due to slow damage to the integrity of the vascular wall. Most frequently, perforation has a delayed course and results from endothelial injury caused by the hyperosmolar fluids, leading to transmural necrosis and thrombosis.

The risk appears to be greatest when the end of the catheter creates an acute angle to the vessel or cardiac wall. This may then cause injury because a jet of abrasive fluid is directed at a small area of the wall, assisted by reactive thrombus attaching the catheter tip to the endothelium. This is most likely to happen with:

(a) A redundant length of free catheter in the heart (for PCE); or (b) a catheter tip in the left innominate vein at its junction with the superior vena cava[4]. Subsequently, the fluid diffuses transmurally across the myocardium into the pericardium.

It usually presents as a sudden, unexplained cardiac arrest and sometimes it can present as unexplained cardio-respiratory instability such as hypotension, bradycardia and desaturation[4]. The picture was the similar in our case. It is estimated that "a volume of 11.4 ± 1.5 ml/kg body weight is enough to result in tamponade"[5]. In our case we could remove 32 ml/kg aspirate, which was similar in composition to the infusate.

Several risk factors have been proposed that increase the risk of PCE with cardiac tamponade in a neonate with CVC, namely, (a) Neonatal cardiac atrium is more susceptible to damage as some areas have very little musculature, (b) PCE is most commonly described with catheter tips placed within cardiac outline, though extra-cardiac positioning does not completely abolish the risk of PCE, and (c) Catheter inserted *via* neck or arm vein have more chances of migration which increases the risk of PCE[6].

Polyethylene or polyurethane catheters in contrast to silastic catheters have more risk of PCE[6,7]. The food and drug administration (FDA) of the United States of America recommends that for safe placement of CVC "the catheter tip position should be confirmed by X-ray or other imaging modality and rechecked periodically[8].

CONCLUSION

PCE and cardiac tamponade should be considered in any infant with a central venous line who develops a rapid, unexplained clinical deterioration.

PCE is most commonly described with catheter tips placed within cardiac outline, though extra-cardiac positioning does not completely abolish the risk of PCE. As migration of the catheter tip can occur, we suggest that its position should be checked immediately after insertion and bi-weekly, thereafter.

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Case Report

Incomplete Small Bowel Obstruction Caused by Idiopathic Diaphragm Disease of the Proximal Ileum

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ABSTRACT

Diaphragm disease is a rare pathology and describes the phenomenon of circumferential, concentric mucosal lesions of the bowel which can cause progressive narrowing of the bowel lumen and bowel obstruction. The etiology in significant majority of cases is previous or concurrent ingestion of non-steroidal anti-inflammatory drugs (NSAID).

A 55-year-old Caucasian man with no history of prior ingestion of NSAID presented with a three week history of progressive abdominal pain, distension and subsequent absolute constipation. He failed a trial of conservative management and subsequently underwent a laparotomy and small bowel resection for small bowel obstruction. Histopathological analysis revealed diaphragm disease of the small bowel.

This case emphasizes the complexities in the management of patients with incomplete small bowel obstruction and highlights the possibility of diaphragm disease of the bowel in the absence of known risk factors.

KEY WORDS: gastroenterology, general surgery, diaphragm disease

INTRODUCTION

Diaphragm disease (DD) is a rare pathology of the gastrointestinal tract, most commonly affecting the small bowel. It is characterized by concentric mucosal lesions ('diaphragms') within the bowel which reduce the diameter of the bowel lumen[1]. Although the pathogenesis of the condition is still unclear, non-steroidal anti-inflammatory drug (NSAID) use is considered as the most common predisposing factor[1]. This case report describes a patient with no known predisposing risk factors who developed diaphragm disease of the small bowel.

CASE PRESENTATION

A 55-year-old Caucasian man presented to the Emergency Department (ED) of a district general hospital with a three-week history of colicky, central abdominal pain. He had not passed flatus for 48 hours. He had vomited once, two days prior to admission and reported a reduced appetite and significant weight loss over the course of his illness. His past medical history included chronic leg pain since an accident 35 years ago and he required regular co-codamol (30/500 mg, QDS). He also admitted to intravenous drug abuse many years earlier. He reported no previous or recent use of NSAID analgesia and no history of inflammatory bowel disease.

Physical examination revealed tenderness in the peri-umbilical region and soft abdominal distension. He had no clinical signs of peritonism and his bowel sounds were audible, though high-pitched. He had no palpable herniae and no palpable masses or organomegaly. Hematological investigations revealed a microcytic anemia (Hemoglobin = 9.0 g/dl, Mean Cell Volume = 63 fl). Plain abdominal radiographs revealed small bowel obstruction (Fig. 1). Urgent computed tomography (CT) imaging was performed which confirmed dilated, fluid filled small bowel loops but also gas and feces in the large bowel with no transition point of true obstruction in the small bowel.

Initial management was conservative in nature with nasogastric decompression of the stomach, careful fluid balance and intravenous fluid infusion. His condition worsened and he vomited one liter of feculent fluid four days after admission. He proceeded to emergency laparotomy where the small bowel was dilated proximal to a single, well-defined transition point in the proximal ileum. There was no evidence of inflammatory bowel disease or carcinoma and no extrinsic compression. An intra-luminal stricture

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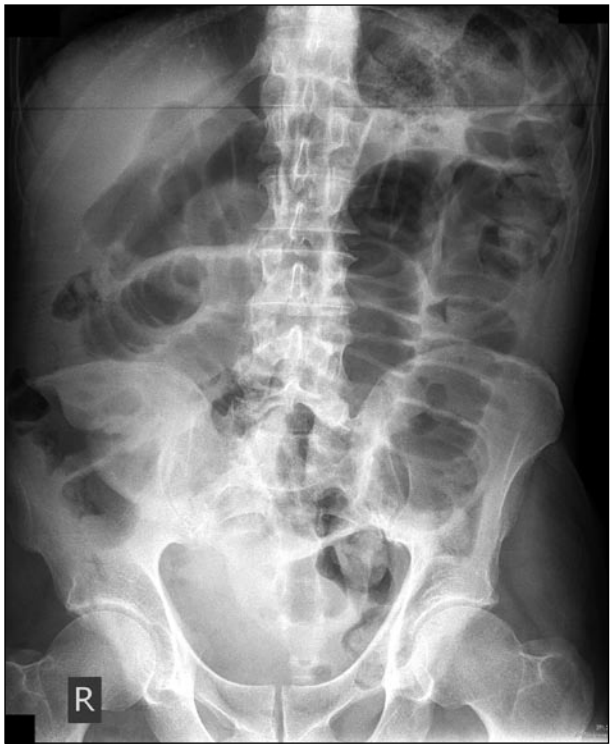

Fig. 1: Plain supine abdominal radiograph which demonstrates dilated small bowel consistent with small bowel obstruction

was found at the point of transition with a patent, but very narrow lumen. Similar constrictions were noted throughout the length of the small bowel but the patency of the lumen was not compromised at these areas. A wedge resection of the affected area of small bowel was performed and stapled side-to-side anastomosis using the TLC 75 (Ethicon, UK) device was fashioned. He made a good post-operative recovery and was discharged home four days after surgery.

Histopathological examination of the resected specimen revealed the presence of an intra-luminal diaphragm within the small bowel consisting of prominent hyperplastic folds with intervening stromal cells, consistent with diaphragm disease of the small bowel (Fig. 2). The diaphragm consisted of significant fibrosis, which was confined to the submucosal layer with minimal mucosal ulceration. This was confirmed on both hematoxylin and eosin staining and Van Gieson's staining. There was a slightly greater density of neutrophil polymorphs and lymphocytes at the areas of mucosal ulceration. There was no evidence of any other pathology; in particular, there was no evidence of Crohn's disease, malignancy or other inflammatory bowel disease and specific immune-histochemistry stains were not performed.

DISCUSSION

DD was first described in 1988[1] as circumferential mucosal lesions forming "diaphragms" within the small bowel. The small bowel is most commonly

Fig. 2: Histopathological analysis of intra-luminal diaphragm within the small bowel consisting of prominent hyperplastic folds with intervening stromal cells

affected although similar lesions have been reported in the colon[2]. Histologically, diaphragms are similar to the normal plicae circulares in the small bowel but with submucosal fibrosis, and occasional mucosal ulceration and villous atrophy[1].

There is a clear association between DD and long-term NSAID use and NSAIDs are known to affect enterocytes directly by increasing intestinal permeability[3], which might allow bacterial invasion of the bowel wall with secondary inflammation. DD in the absence of NSAID use is very rare although unknown NSAID ingestion was possible in these cases[2,4]. In this case, given the long term management of chronic leg pain, formal documentation of analgesics prescribed both in the community and hospital settings was available and we are confident that there was no prior NSAID use. We are unsure as to the etiology of diaphragm disease in this case and, on histopathological analysis, there was no chronic inflammation or ulceration, suggesting that systemic factors may have a role.

Radiological investigations, as in this case, can be misleading and can often overlook intra-luminal diaphragms. The diagnosis is usually confirmed on histopathological analysis although can be suspected from other imaging techniques such as capsule endoscopy, small bowel enteroscopy, small bowel contrast studies or enteroclysis. The tendency for objects to be retained within diaphragm compartments themselves may also be useful for diagnosis[5].

Progressive obstruction caused by diaphragm disease requires surgical resection of the affected bowel and strictuloplasty-type operations are of no benefit given the circumferential nature of the disease. There is no current guidance on the management of other diaphragms found at surgery. In this case, resection was not possible given the length of bowel that was affected and as such an intra-operative decision to leave bowel that had a patent lumen was taken and

this seems to be an appropriate management plan. In addition, the patient was fully informed of his final pathology to allow rapid assessment and management, should he develop signs of small bowel obstruction in future.

CONCLUSIONS

DD of the bowel is a rare condition. It should be considered in the differential diagnosis of intestinal obstruction in a virgin abdomen. Ingestion of NSAIDs has been associated with this disease although no history of NSAID ingestion was found in the case presented in this report.

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Case Report

Dengue Fever among Travelers

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ABSTRACT

Dengue fever, also known as break bone fever, is an acute life-threatening febrile illness, which usually occur in the tropical and subtropical areas. Travelers may both acquire and spread dengue virus infection. We report a case of Dengue fever in a traveler from an endemic area. In this case report, we will emphasize the clinical manifestations and diagnosis of dengue virus infection from other tropical diseases affecting people who have recently travelled. It is important that health care providers and travelers be aware of such infections for proper management and prevention.

KEY WORDS: fever, mosquitos, tropical diseases

INTRODUCTION

Dengue fever is one of the tropical diseases reported by travelers[1]. It is transmitted by Aedes mosquito. Among 20 to 70 percent of 50 million travelers between industrialized countries to developing countries each year report some illness associated with their travel[1]. Although most illnesses are mild, 8 percent require medical care[2]. This depends on several factors. People who visit family and local homes have an increased chance of exposure to pathogens than tourists[1].

After an incubation period of seven days, dengue fever manifests as an influenza like illness with fever, headache, and myalgia. In 50 percent of the infected people, diffuse maculopapular rash and petechial rash develop. Other clinical manifestations include lymphadenopathy, mild respiratory and gastrointestinal symptoms, in addition to hemorrhagic manifestations[1,3]. Classic dengue fever in travelers is self limiting and rarely fatal. It may require hospitalization. We present a classic case of dengue fever in a traveler from an endemic area.

CASE REPORT

A 63-year-old Canadian male of Pakistani origin presented to our medical casualty with three days history of high-grade fever, vomiting and diarrhea, followed by altered mental status on the day of admission. He was known to be diabetic, hypertensive and was diagnosed to have bronchial asthma. His family had noted a decrease in his conscious level for one day before they sought medical advice. The patient had come back from Pakistan a week ago. There were no ill contacts at home. He gave history of a recent urinary tract infection that was treated in Pakistan. He also gave a history of anti-pyretic tablet consumption (eight pills over two days) to relieve his fever.

On presentation, his temperature was 39.6 °C. His respiratory rate and heart rate were 20 breaths, 94 beats per minute respectively. His blood pressure was measured to be 153 / 85 mmHg. He was conscious, but drowsy and disoriented. He appeared jaundiced. His abdomen was distended secondary to a quickly developing ascites. A diffuse, non-blanching, confluent rash was present on his upper and lower limbs. (Fig. 1-3) He had mild right upper quadrant tenderness. The rest of his physical examination was unremarkable. His laboratory work up revealed mild anemia, a hemoglobin of 120 g/l, and thrombocytopenia with a platelet count of 19,000. He had leucopenia with a WBC count of 2.1 x 109/ml. His coagulation profile was prolonged.

During the patient's stay in the hospital, he developed worsening of all his laboratory parameters. He developed a marked drop in his hemoglobin to 90 g/l. His liver function tests and liver enzymes were deteriorating. His total bilirubin (TBil) was 113 mmol/l, Aspartate Transaminase (AST) 2349 mmol/l, Alanine Transaminase (ALT) 1567 mmol/l, Gamma Glutamate (GGT) 191 mmol/l. His Albumin level was 27 g/l. Serial screen for tropical diseases such as malaria, typhoid fever and brucella was negative. An enzyme-linked immunosorbent assay (ELISA)

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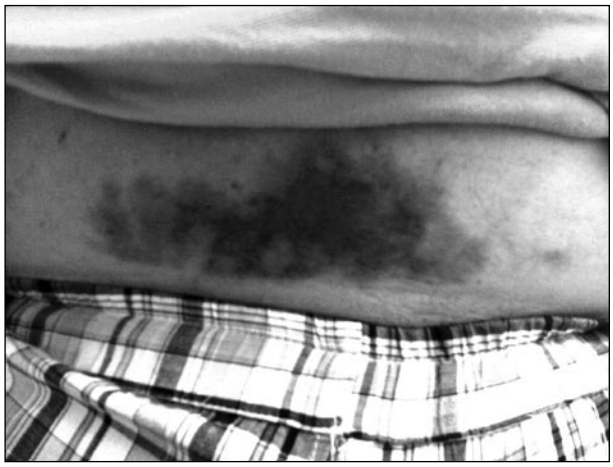

Fig. 1: Maculopapular rash involving the abdomen

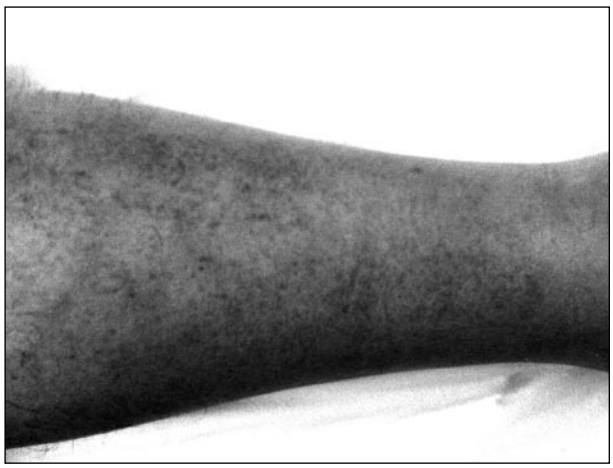

Fig. 2: Peticheal rash over the right lower limb

test was performed to detect viral causes showed positive results for Dengue virus immunoglobulin M (IgM) and for Dengue virus immunoglobulin G (IgG). Otherwise, his serum was negative for Hepatitis A virus immunoglobulin M (HAV AB IgM), Hepatitis B virus surface Antigen (HBsAg), and Hepatitis C virus antibodies. The tests were carried out in the virology laboratory in Mubarak Al-Kabeer hospital. Dengue IgM and IgG Capture Elisa were used to isolate the immunoglobulin through panbio-diagnostics. The patient was treated conservatively with good hydration using intravenous fluids, and he was transfused with blood and fresh frozen plasma.

DISCUSSION

The clinical suspicion of Dengue fever, as in our case, depends on a triad of symptoms and signs, namely, the hemorrhagic manifestation evident as petechial rash, in addition to low platelet count and plasma leakage, as in pleural or ascitic fluid[3]. Our patient had a low platelet count and ascitic fluid, with the history of recent travel. This increased our suspicion of Dengue virus infection. Other tropical

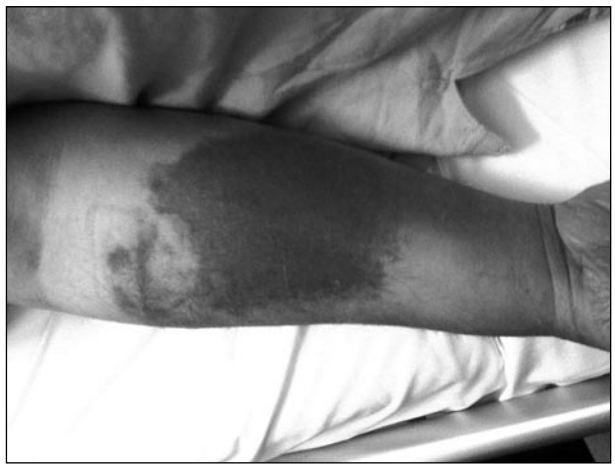

Fig. 3: Ecchymosis of the right forearm

diseases should be suspected, such as malaria, typhoid fever, leptospirosis, and other illnesses that can manifest in the acute phase as undifferentiated febrile syndrome. The most serious forms of infection are Dengue shock syndrome, which is characterized by weak pulse and profound hypotension and dengue hemorrhagic fever. The mortality rate can go up to 40 percent[3]. However, this is rare among travelers[1,4].

The pathogenesis of hemorrhagic fever is capillary leakage, associated with hemorrhagic manifestations. The plasma leak develops within the first four to seven days after the onset of the disease and manifests as pleural effusion, ascites and hypoproteinemia.

Laboratory tests were helpful in the diagnosis. Specific tests such as polymerase chain reaction (PCR), cultures and serological assay would confirm the diagnosis[3,4]. Other laboratory findings that supported our diagnosis were the low platelet counts, leukopenia and the increased liver aminotransferase levels. An increased hemotocrit of 20 percent may suggest plasma loss[1,3].

The treatment is based on supportive measures and prompt restoration of circulating plasma volume is the cornerstone of therapy of dengue fever and its complications[5,6]. Other supportive measures such as bed rest and antipyretics can be used. If there is evidence of bleeding or disseminated intravascular coagulation, blood and fresh frozen plasma should be administered[1,3,5].

The fluid restoration should be tapered down when the hematocrit decreases by 40 percent in order to avoid complications of fluid overload. The risk of acquiring dengue fever is high in immune-compromised patients.

For prevention of dengue fever, travelers should avoid mosquito bites in endemic areas. A vaccine that provides immunity against all four serotypes of dengue is needed and this is still under clinical trial[3,7].

CONCLUSION

Dengue fever is a disease of travelers to endemic areas. Although the virus is uncommon in Kuwait, it should be suspected in acute febrile illness with a history of recent travel. It is characterized by vascular leakage and disordered homeostasis. Initial resuscitation is with fluids bed-rest and antipyretics in mild disease to plasma and blood products in severe hemorrhagic dengue and shock .

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Case Report

Bilateral Massive Angiomyolipomatosis Associated with Tuberous Sclerosis

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ABSTRACT

Angiomyolipoma is an uncommon tumor consisting of vascular, smooth muscle, and fatty elements. Angiomyolipoma can present in two forms; as an isolated unilateral lesion which occurs sporadically or as bilateral lesions associated with tuberous sclerosis and Von Hippel-Lindau syndrome. Bilateral massive angiomyolipomatosis is a very rare entity. Only three cases have been reported in medical literature. We present a case of bilateral massive angiomyolipomatosis associated with tuberous sclerosis.

KEY WORDS: angiomyolipomatosis, massive hemorrhage, tuberous sclerosis

INTRODUCTION

Tuberous sclerosis is a relatively rare disease with an incidence of 1:100,000[1]. Renal angiomyolipoma is an uncommon lesion, comprising about 0.3% of all renal masses[1]. Angiomyolipoma can present as unilateral, solitary lesion, which occurs with a higher female predisposition in middle age (M: F = 4:11) or as bilateral, multiple lesions of various sizes associated with tuberous sclerosis or Von Hippel–Lindau syndrome[1]. About 20% of angiomyolipomas are associated with tuberous sclerosis and about 80% of tuberous sclerosis patients have angiomyolipomas[2,3]. Bilateral massive angiomyolipomatosis is a very rare entity, with only three case reports in medical literature; all the three being associated with tuberous sclerosis[4-6]. Angiomyolipomas can remain asymptomatic or present with fever, nausea, vomiting, mass, abdominal distension, abdominal pain, flank pain, gross hematuria, renal failure, anemia or hemorrhage[7,8]. The presentation can be delayed due to poor communication as a result of mental retardation, thus increasing the morbidity and mortality. Thus a high index of suspicion is needed in mentally retarded patients with poor communication skills, especially for the prompt intervention of spontaneous hemorrhage. We report this very rare case to increase the awareness so as to reduce the associated mortality and morbidity due to delay in diagnosis in similar cases.

CASE REPORT

A 33-year-old mentally retarded male patient was brought to the emergency department with one day history of severe abdominal pain and vomiting. Clinical examination revealed a pale patient with tachycardia and severe hypotension (60/50 mmHg). Resuscitative measures were initiated. A large mass was felt occupying most of his abdomen, along with fullness in both flanks. The patient was known to have tuberous sclerosis with mental retardation and epilepsy. Hematological investigations revealed anemia (Hb 97 g/l) and renal impairment (serum creatinine 219 μmol/l). There was further rapid drop in Hb to 67g/l and worsening of renal impairment with serum creatinine rising to 314 μmol/l. An urgent non-enhanced CT-scan of the abdomen and pelvis was done which showed bilateral huge heterogeneous masses with fat and soft tissue attenuation in the retroperitoneum occupying the renal areas and replacing the normal renal parenchyma (Fig. 1a, 1b). There was high attenuation suggestive of hemorrhage, fluid level and extensive fat-stranding in the right side mass (Fig. 1a). Prominent linear structures suggestive of extensive abnormal vasculature were seen (Fig. 1b, 1c). The masses displaced the bowel anteriorly (Fig. 2). The mass on the right side measured 24.3 cm x 20.9 cm x 16.6 cm (Fig. 3a, 3b) and on the left measured 32.6 cm x 19.6 cm x 13.8 cm (Fig. 3c, 3d). The findings were diagnostic of bilateral massive angiomyolipomas with

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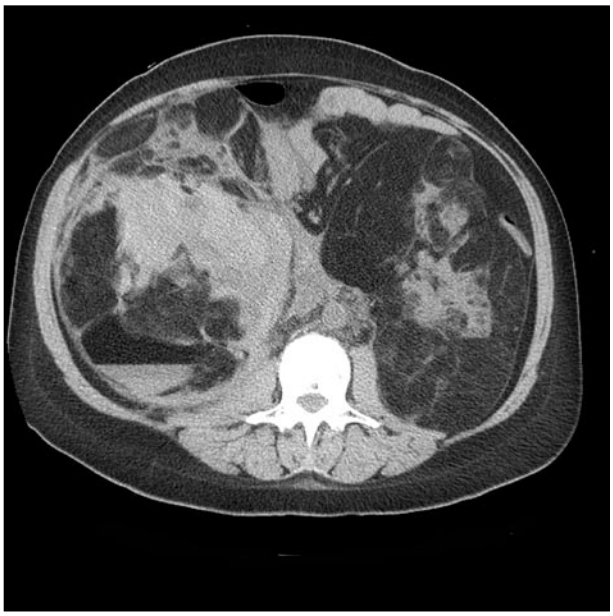

Fig. 1a: Non-enhanced axial CT scan showing bilateral huge heterogeneous masses with fat and soft tissue attenuation in the retroperitoneum occupying the renal areas and replacing the normal renal parenchyma; along with high attenuation suggestive of hemorrhage, fluid level and extensive fat-stranding in the right side mass

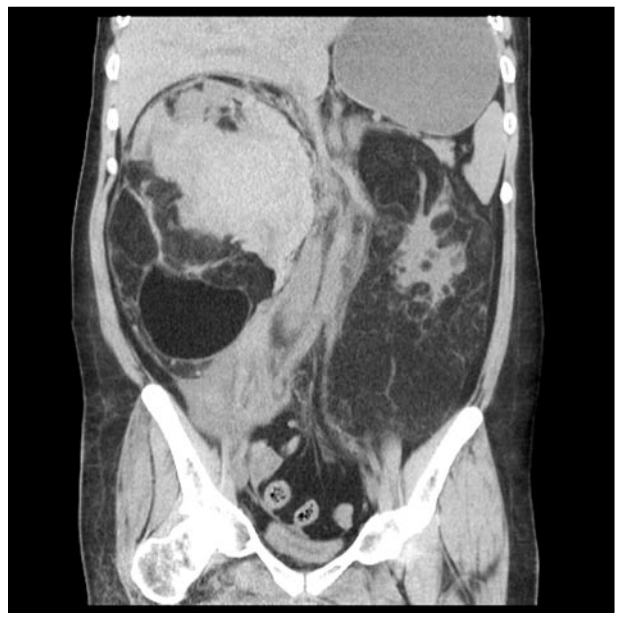

Fig. 1c: Coronal reconstruction of non-enhanced CT scan showing prominent linear structures suggestive of extensive abnormal vasculature

hemorrhage on the right. The patient was stabilized by giving blood transfusion and IV fluids and was posted for selective arterial embolization, and if needed nephrectomy. Unfortunately the patient had cardiac arrest most probably due to hypovolemic shock as a result of continuing hemorrhage and died in spite of attempted resuscitation.

DISCUSSION

Tuberous sclerosis is a rare autosomal dominant disorder with variable penetrance The incidence is approximately 1 in 100,000 with equal distribution in both sexes[8, 9]. Classically, the disease is described as a clinical triad of adenoma sebaceum, mental retardation and seizures. However, due to incomplete

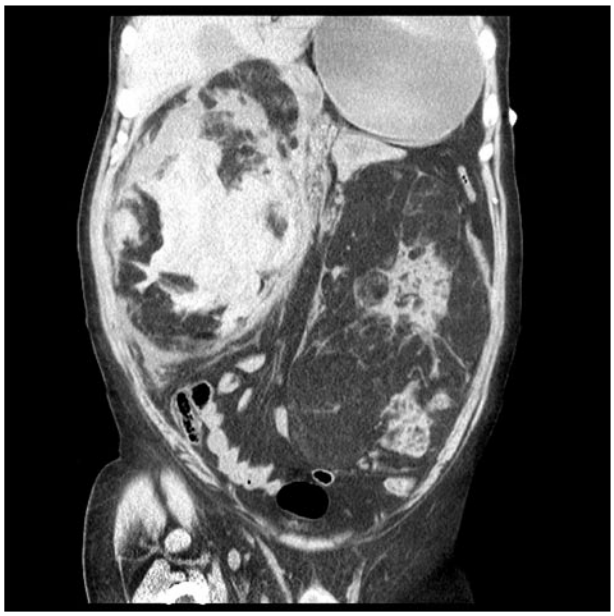

Fig. 1b: Coronal reconstruction of non-enhanced CT scan showing bilateral huge heterogeneous masses with fat and soft tissue attenuation; along with prominent linear structures suggestive of extensive abnormal vasculature on the left

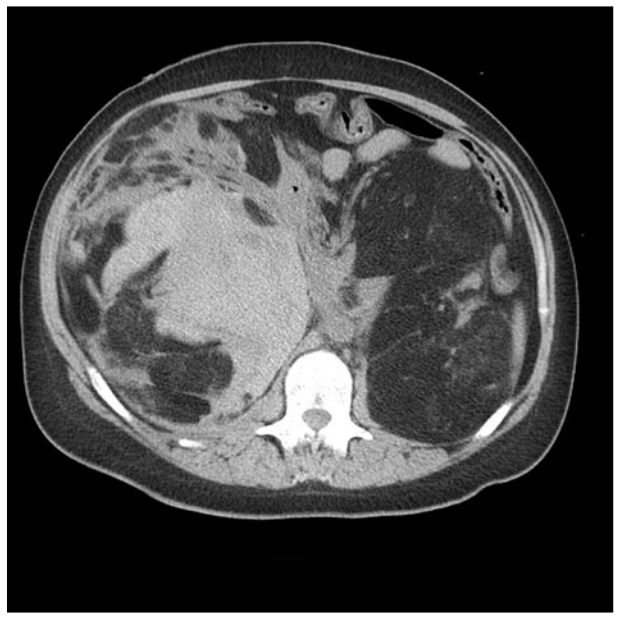

Fig. 2: Non-enhanced axial CT scan showing anterior displacement of the bowel loops by the mass

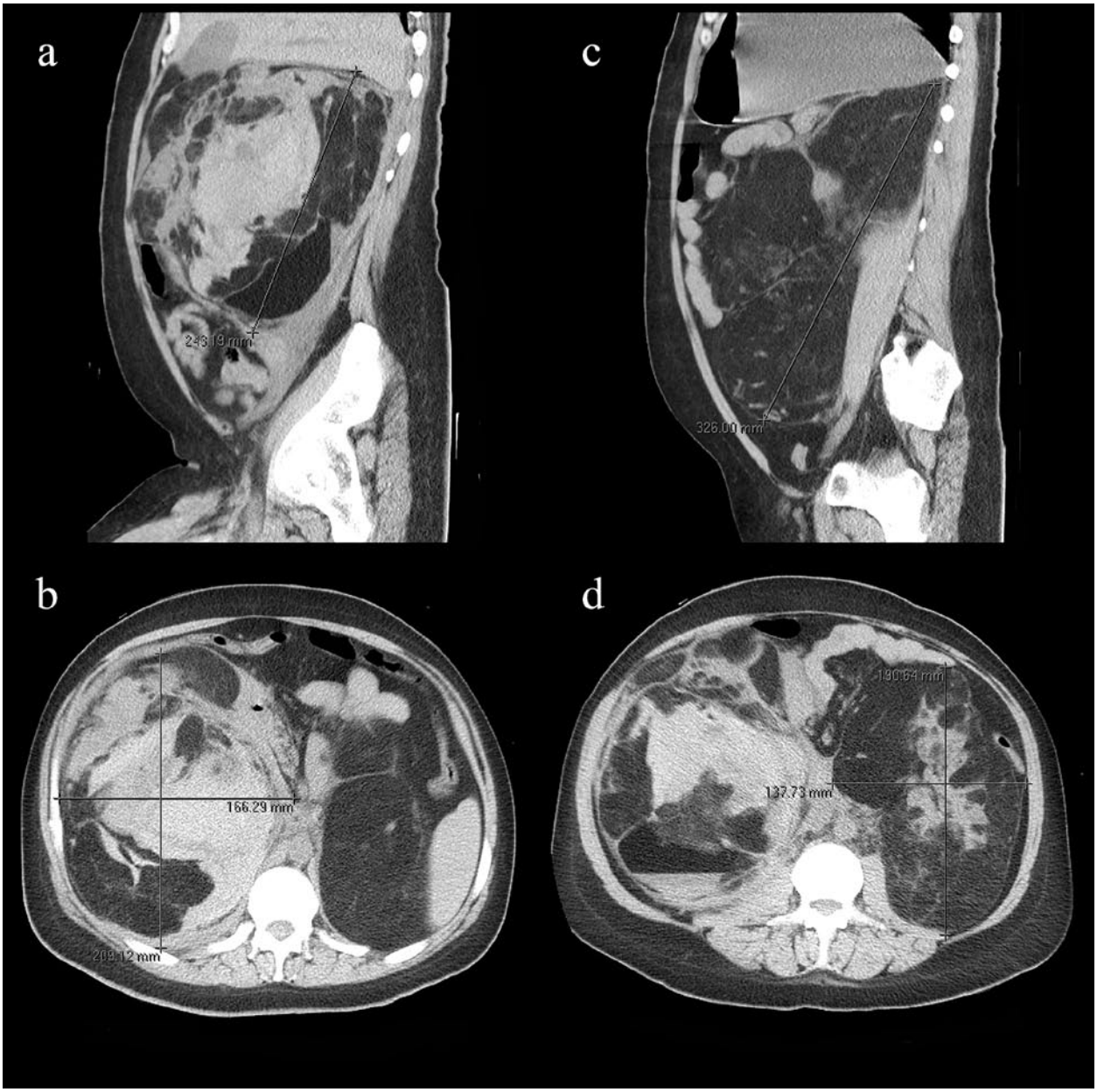

Fig. 3a, 3b, 3c, 3d: Non-enhanced axial and coronal CT images showing size of the masses

penetrance, symptomatology may range from isolated organ involvement present in mild incomplete disease, to involvement of multiple organs. The patients with tuberous sclerosis can have glial tumors of the brain, rhabdomyoma of the heart, and hamartomatous tumors of the thyroid, retina, liver, pancreas, lung, kidney, adrenals and ovaries[10,11]. Angiomyolipoma can present as unilateral, solitary lesion, which occurs with a higher female predisposition in middle age (M: F = 4:11) or as bilateral, multiple lesions of various sizes associated with tuberous sclerosis or Von Hippel-Lindau syndrome[1]. About 20% of angiomyolipomas are associated with tuberous sclerosis and about 80% of tuberous sclerosis patients have angiomyolipomas[2, 3]. Thus, the most common association of angiomyolipoma is with tuberous sclerosis and there are four times as many sporadic angiomyolipomas as there are cases associated with tuberous sclerosis.

Angiomyolipoma is a benign renal neoplasm composed of vascular smooth muscle and fatty elements. The demonstration of fat on ultrasound and CT can accurately diagnose angiomyolipoma in 95% of the cases and is pathognomonic[12,13]. In our case, the diagnosis of angiomyolipoma was made on the basis of CT scan which showed fat, hemorrhage and prominent abnormal vascularity. The renal angiomyolipomas usually remain silent and are incidental findings at autopsy[14]. However, they may present with fever, nausea, vomiting, mass, abdominal distension, abdominal pain, flank pain, gross hematuria, renal failure,

anemia or hemorrhage[7, 8]. Our patient had abdominal pain, vomiting, mass, anemia and retroperitoneal hemorrhage. Patients with angiomyolipoma associated with tuberous sclerosis present at a younger age, are more likely to be symptomatic, have large bilateral tumors that are more likely to grow and therefore more frequently require surgery. In the series by Steiner *et al*[15], the average size of angiomyolipoma in patients with tuberous sclerosis was 9.6 ± 4.8 cm, and in those without tuberous sclerosis, was 4.1 ± 3.4 cm. Angiomyolipoma may grow to be large and bulky and extend into the perirenal space, which sometimes makes it difficult to differentiate from perirenal liposarcoma. However, perirenal liposarcoma is unilateral and usually spares the architecture of the kidney because it arises from retroperitoneal fat. In comparison, renal angiomyolipoma arises from the renal parenchyma and involves the kidney itself[16]. Our patient had bilateral massive angiolipomatosis, the renal parenchyma being inseparable from the lesion. The mass on the right side measured 24.3 cm x 20.9 cm x 16.6 cm and on the left measured 32.6 cm x 19.6 cm x 13.8 cm. Only three cases of bilateral massive renal angiomyolipomatosis have been mentioned in the literature[4-6]. In comparison with those cases, our case happens to be the second biggest.

Most angiomyolipomas can be managed conservatively, particularly if they are asymptomatic. Nephron conservation is of great importance in tuberous sclerosis, as the tumors are often bilateral. Partial nephrectomy is ideal for masses with a diameter smaller than 3 cm, and partial nephrectomy may be possible in masses with a diameter smaller than 5 cm that do not reach the hilum. Lesions greater than 3.5 - 4 cm size are at great risk of serious spontaneous hemorrhage. Renal arterial embolization can be used to control the hemorrhage. When the lesions are greater than 10 cm, preferred treatment is partial nephrectomy or selective arterial embolisation[12,15]. Our patient was posted for selective arterial embolization and if needed nephrectomy. Unfortunately the patient had cardiac arrest most likely due to hypovolemic shock as a result of continuing hemorrhage from the angiomyolipoma and died in spite of attempted resuscitation. Of the three cases of bilateral massive renal angiomyolipamatosis mentioned in literature, two patients presented with hemorrhage; one of these patient who had nephrectomy survived[4], while the other patient who did not undergo surgery died due to massive hemorrhage[5]. In general, individuals with mild form of disease live well with good life expectancy, while those with severe form of disease have serious disabilities. However, with appropriate management most individuals have normal life expectancy[17]. Lesions large than 3.5 - 4 cm are associated with catastrophic hemorrhage leading to death unless appropriately treated[12, 5]. The leading causes of death include renal failure, brain tumor, status epilepticus, bronchopneumonia and lymhangiomyomatosis[18].

CONCLUSION

Renal angiomyolipomas associated with tuberous sclerosis are distinctly different from those without tuberous sclerosis. Patients with renal angiomyolipomas associated tuberous sclerosis present at a younger age, are, more likely to be symptomatic, have large bilateral tumors that are more likely to grow and therefore more frequently require surgery. Bilateral massive angiomyolipomatosis is a very rare entity, with only three case reports in medical literature; all the three being associated with tuberous sclerosis. Angiomyolipomas can have varying clinical presentations including life threatening massive hemorrhage. Poor communication as a result of mental retardation in these patients can delay the diagnosis, resulting in increased morbidity and mortality. Thus a high index of suspicion is needed in mentally retarded patients with poor communication skills, especially for prompt intervention for spontaneous hemorrhage.

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Letter to the Editor

Evaluation of Lamivudine Effect on Prevention of Hepatocellular Carcinoma Recurrence

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Limited information is available about the effect of lamivudine treatment on prevention of hepatocellular carcinoma (HCC) recurrence in Taiwan. This was a hospital-based observational study. We analyzed the medical records of subjects with HCC initially treated by hepatic resection, were hepatitis B surface antigen (HBsAg) positive and hepatitis C antibody positive, at one medical center in Taiwan from 2000 to 2008. The institutional review board of this medical center approved this retrospective study. In all, seven subjects received 100 mg/day lamivudine after hepatic resection (lamivudine group) and 39 subjects underwent hepatic resection only (control group). The overall follow-up period was 52 weeks. There were no significant differences in gender, age, aspartate aminotransferase, alanine aminotransferase, total bilirubin, albumin, alpha-fetoprotein, platelet count, prothrombin time, presence of ascites, Child–Pugh score, HCC pathological grade[1] and cancer of the liver Italian program (CLIP) score[2] between the control group and the lamivudine group at the time of HCC diagnosis. The mean periods from initial treatment to recurrence were 32.3 ± 17.5 weeks (range 5 to 52) in the control group and 31.3 ± 20.6 weeks in the lamivudine group (range 7 - 52) ($p = 0.890$). During the follow-up period, out of the 46 subjects, 24 subjects (52.2%) experienced HCC recurrence at the end of 52 weeks (21 subjects in the control group and three subjects in the lamivudine group). The cumulative recurrence rates of HCC at 26 and 52 weeks in the control group were 33.3% and 53.8%, respectively, while those in the lamivudine group were 28.6% and 42.9%, respectively. There were no significant differences regarding the recurrence rates of HCC between two groups ($p = 0.82$).

To date, there are few reports regarding the effects of antiviral therapy on recurrent HCC. Two studies in Japan have disclosed that the cumulative recurrence rates of HCC did not significantly differ between the lamivudine group and the control group[3,4], which was compatible with this present study. In Kim's study, lamivudine therapy could increase albumin, decrease ascites and decrease Child-Pugh score in patients with hepatitis B virus-related HCC[5]. The author concluded that lamivudine therapy could increase the curative chance in patients with hepatitis B virus-related HCC[5].

To date, according to the above literature[3,4] and this present study, lamivudine therapy seems to be not effective in prevention of HCC recurrence after resection of primary tumor. However, because this present study is a small sample size, we cannot make a strong recommendation about the effect of lamivudine therapy. A larger sample size is needed to confirm whether antiviral drugs can improve the recurrence rate.

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4. Piao CY, Fujioka S, Iwasaki Y, *et al*. Lamivudine treatment in patients with HBV-related hepatocellular carcinoma - using an untreated, matched control cohort. Acta Med Okayama 2005; 59:217-224.
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Selected Abstracts of Articles Published Elsewhere by Authors in Kuwait

Kuwait Medical Journal 2012, 44 (2): 155 - 158

Combined Pelvic Osteotomy for the Bipartite Acetabulum in Late Developmental Dysplasia of the Hip, A Ten-Year Prospective Study

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J Bone Joint Surg Br 2011; 93-B:257-261

In late developmental dysplasia of the hip in childhood, the deformed dysplastic acetabulum is malaligned and has lost its shape due to pressure from the subluxed femoral head. The outer part of the acetabulum involves the upper part of the original acetabulum, thereby giving a bipartite appearance. A clear edge separates the outer from inner part which represents the lower part of the original acetabulum and has no direct contact with the femoral head.
Combined pelvic osteotomy (CPO) using a Lance acetabuloplasty with either a Salter or a Pemberton procedure restores the original shape and realigns the acetabulum. A total of 20 children (22 hips), with a mean age of 46 months (28 to 94) at primary operation underwent CPO with follow-up for between 12 and 132 months.
In each case concentric stable reduction with good acetabular cover was achieved and maintained throughout the period of follow-up.

Identification of Two Novel CAKUT-Causing Genes by Massively Parallel Exon Resequencing of Candidate Genes in Patients with Unilateral Renal Agenesis

Saisawat P, Tasic V, Vega-Warner V, Kehinde EO, Günther B, Airik R, Innis JW, Hoskins BE, Hoefele J, Otto EA, Hildebrandt F
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Kidney Int 2012; 81:196-200

Congenital abnormalities of the kidney and urinary tract (CAKUT) are the most frequent cause of chronic kidney disease in children, accounting for about half of all cases. Although many forms of CAKUT are likely caused by single-gene defects, mutations in only a few genes have been identified. In order to detect new contributing genes, we pooled DNA from 20 individuals to amplify all 313 exons of 30 CAKUT candidate genes by PCR analysis and massively parallel exon resequencing. Mutation carriers were identified by Sanger sequencing. We repeated the analysis with 20 new patients to give a total of 29 with unilateral renal agenesis and 11 with other CAKUT phenotypes. Five heterozygous missense mutations were detected in 2 candidate genes (4 mutations in FRAS1 and 1 in FREM2) not previously implicated in non-syndromic CAKUT in humans. All of these mutations were absent from 96 healthy control individuals and had a PolyPhen score over 1.4, predicting possible damaging effects of the mutation on protein function. Recessive truncating mutations in FRAS1 and FREM2 were known to cause Fraser syndrome in humans and mice; however, a phenotype in heterozygous carriers has not been described. Thus, heterozygous missense mutations in FRAS1 and FREM2 cause non-syndromic CAKUT in humans.

Three Distinct Clones of Carbapenem-Resistant Acinetobacter Baumannii with High Diversity of Carbapenemases Isolated from Patients in Two Hospitals in Kuwait

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J Infect Public Health 2012; 5:102-108

Objectives: This study was undertaken to investigate the clonal relatedness of multidrug-resistant (MDR) Acinetobacter baumannii isolates collected from patients in two teaching hospitals in Kuwait.
Materials And Methods: Clinically significant consecutive isolates of A. baumannii obtained from patients in the Mubarak (36) and Adan (58) hospitals over a period of 6 months were studied. These isolates were identified using molecular methods, and their antimicrobial susceptibility was determined by the Etest method. The mechanism of resistance to carbapenem was investigated by PCR, and pulsed-field gel electrophoresis (PFGE) was used to determine the clonal relatedness of MDR isolates.
Results: Of the 94 isolates investigated, 80 (85.1%) were multidrug resistant (MDR). The A. baumannii PFGE clone A and subclone A1 were the most prevalent in patients infected with MDR isolates. Fifty-five (94.8%) and 15 (41.7%) of the MDR isolates from the Adan and Mubarak hospitals, respectively, belonged to PFGE clone A; isolates in this group showed higher resistance rates to antibiotics than isolates form other groups. Of the 94 isolates, 40 (42.6%) were resistant to either imipenem or meropenem or to both (CRAB). Most CRAB isolates (29/40 or 72.5%) carried bla genes, which code for MBL (VIM-2 and IMP-1) enzymes. Two isolates harbored bla(OXA-23).
Conclusion: Three distinct clones of CRAB were isolated, providing evidence of a high diversity of carbapenemases among our geographically related isolates.

A Study of the Microbiology of Diabetic Foot Infections in a Teaching Hospital in Kuwait

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J Infect Public Health 2012; 5:1-8

The purpose of this study was to determine the microbiological profile of diabetic foot infections (DFIs) and assess the antibiotic susceptibility of the causative agents. Data were obtained from a retrospective analysis of DFI samples collected from June 2007 to July 2008. Specimens were cultured using optimal aerobic and anaerobic microbiological techniques, and antibiotic susceptibility testing was performed according to the methods recommended by the Clinical and Laboratory Standards Institute (CLSI). Extended-spectrum β-lactamase (ESBL) production was measured using the double disk synergy test and the ESBL Etest. A total of 440 patients were diagnosed with DFIs during this period, and a total of 777 pathogens were isolated from these patients with an average of 1.8 pathogens per lesion. We isolated more Gram-negative pathogens (51.2%) than Gram-positive pathogens (32.3%) or anaerobes (15.3%). Polymicrobial infection was identified in 75% of the patients. The predominant organisms isolated were members of the Enterobacteriaceae family (28.5%), Pseudomonas aeruginosa (17.4%), Staphylococcus aureus (11.8%), methicillin-resistant S. aureus (7.7%), anaerobic Gram-negative organisms (10.8%), and Enterococcus spp. (7%). Vancomycin was the most effective treatment for Gram-positive bacteria, and imipenem, piperacillin-tazobactam and amikacin were the most effective treatments for the Gram-negative bacteria. In conclusion, DFI is common among diabetic patients in Kuwait, and most of the cases evaluated in this study displayed polymicrobial etiology. The majority of isolates were multi-drug resistant. The data gathered in this study will be beneficial for future determinations of empirical therapy policies for the management of DFIs.

Incidence, Aetiology and Resistance of Late-Onset Neonatal Sepsis: A Five-Year Prospective Study

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J Paediatr Child Health 2012 Mar 7. doi: 10.1111/j.1440-1754.2012.02432.x

Aim: Investigate the incidence, etiological pattern and the antimicrobial resistance of late-onset neonatal infections over a period of 5 years.
Methods: Longitudinal audit of neonatal sepsis from January 2005 to December 2009, in the main maternity hospital in Kuwait. Late-onset neonatal infection was defined as the culture of a single potentially pathogenic organism from blood or cerebrospinal fluid from an infant older than 6 days in association with clinical or laboratory findings consistent with infection.
Results: The overall incidence was 16.9 (95% confidence interval: 15.8-18.0) episodes per 1000 live births. The commonest pathogen was coagulase-negative Staphylococcus, 339 (35.7%), while Klebsiella was the most common gram-negative infection, 178 (18.8%). Escherichia coli, Enterococcus and Enterobacter spp were each responsible for 6% of all infections. Candida caused 104 (11.0%) infections. The general pattern of infection remained unchanged over the study period. Case fatality was 11.7% (95% confidence interval: 9.7-13.9%) and was high for Pseudomonas (18.4%) and Candida (22.1%) infections. Approximately 24 and 20% of Klebsiella infections were resistant to cefotaxime and gentamicin, respectively, while 28 and 24% of Escherichia coli infections were resistant to cefotaxime and gentamicin, respectively.
Conclusion: The incidence of late-onset infection in Kuwait is high, resembling that in resource-poor countries. The high incidence coupled with low case fatality provides an example for settings where tertiary care is introduced without strict measures against nosocomial infections. Prevention against nosocomial infections in neonatal units has the potential to further reduce neonatal mortality in these settings.

High Resolution Computed Tomography in Asthma

Khadadah M, Jayakrishnan B, Muquim A, Roberts O, Sinan T, Maradny N, Lasheen I

Oman Med J 2012; 27:145-150

Objectives: High-resolution computed tomography (HRCT) can detect the structural abnormalities in asthma. This study attempts to correlate these abnormalities with clinical and pulmonary function test (PFT) data.
Methods: Consecutive stable asthma patients attending Mubarak Al Kabeer Hospital, Kuwait, were subjected to HRCT during a six month period from July 2004 to December 2004, after initial evaluation and PFT.
Results: Of the 28 cases, sixteen (57.1%) had moderate, 6 (21.4%) had mild and 6 (21.4%) had severe persistent asthma. Thirteen (46.4%) patients had asthma for 1 to 5 years and 12 (42.9%) were having asthma for >10 years. Bronchial wall thickening (57.1%), bronchiectasis (28.6%), mucoid impaction (17.9%), mosaic attenuation (10.7%), air trapping (78.6%) and plate like atelectasis (21.4%) were noted. Bronchial wall thickening ($p = 0.044$) and bronchiectasis ($p = 0.063$) were most prevalent in males. Ten (35.7%) patients exhibited mild, 9 (32.1%) had moderate and 3 (10.7%) had severe air trapping. The difference in Hounsfield units between expiratory and inspiratory slices (air trapping) when correlated with percent-predicted FEV1 in right upper ($r = 0.25$; $p = 0.30$), left upper ($r = 0.20$; $p = 0.41$), right mid ($r = 0.15$; $p = 0.53$), left mid ($r = -0.04$; $p = 0.60$), right lower ($r = 0.04$; $p = 0.86$) and left lower zones ($r = -0.13$; $p = 0.58$) showed no relation. The same when correlated as above with the percent predicted FEF 25-75 did not show any significant association. The presence of air trapping was compared with sex ($p = 0.640$), nationality ($p = 1.000$), disease duration ($p = 1.000$) and severity of symptoms ($p = 0.581$).
Conclusion: Abnormal HRCT findings are common in asthma; however, air trapping when present was not related to the duration or severity of the illness or to the FEV1.

Infectious Etiologies of Transient Neutropenia in Previously-Healthy Children

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[3]Departments of Pediatric Hematology & Oncology, Al-Sabah Hospital

Pediatr Infect Dis J 2012 Mar 12 [Epub ahead of print]

Background: Healthy children presenting with neutropenia are often hospitalized and treated empirically with antibiotics without an evidence of infection. The objective of this study was to investigate the infectious causes of isolated transient neutropenia in otherwise previously- healthy children.
Method: A two-year prospective study was conducted at a tertiary hospital in Kuwait. All previously-healthy children (aged 1 month - 12 years) hospitalized with isolated neutropenia defined as absolute neutrophil count (ANC) ≤ 1.5 x 10/L were enrolled in the study. Investigations to identify the infectious causes included blood and urine culture for bacteria whereas for viruses, serology for EBV, CMV, adenovirus, parvovirus and PCR for HHV6 and enterovirus were performed.
Results: Fifty five children were enrolled during the study. Children less than 2 years constituted 73% of the sample. There were two peaks of presentation: March - May (33%) and September - November (38%). Associated features were: congested throat (56%), runny nose (53%), and cervical lymphadenopathy (20%). The median ANC on admission was 0.6 x 10/L. Associated infections were documented in 55% of enrolled children and were as follows: HHV6 30%, enterovirus 23%, influenza A H1N113%, parvovirus10%, EBV10%, UTI (*E.coli*) 7%, and adenovirus 7%. No serious bacterial infection was identified and the mean time for recovery of the ANC was 16.7 ± 15 days.
Conclusion: Neutropenia in previously-healthy children in Kuwait is caused by demonstrable infections in 55% of cases. Majority of children will recover their ANC completely within one month without significant infectious complications.

Genotypic Heterogeneity and Molecular Basis of 5-Flucytosine Resistance among Candida Dubliniensis Isolates Recovered from Clinical Specimens in Kuwait

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Department of Microbiology, Kuwait University, Kuwait

Med Mycol 2012; 50:244-251

There is a paucity of information about genotypic heterogeneity among Candida dubliniensis isolates recovered from different geographic regions. This study explored genotypic heterogeneity among 103 C. dubliniensis strains obtained over a six-year period from clinical specimens in Kuwait. Genotype assignment was based on amplification with genotype-specific primers and sequencing of rDNA. Susceptibility to 5-flucytosine was determined by means of the Etest. DNA sequencing of cytosine deaminase was performed to determine the molecular basis of resistance to 5-flucytosine. DNA sequencing of rDNA identified seven different genotypes, *i.e.*, 68 (66%) isolates were found to belong to genotype 1, 25 to genotype 4, six to genotype 5 and one each to genotypes 6-9. Strains of genotype 2 or genotype 3 were not detected. All isolates of genotype 4 but none of other genotypes were resistant to 5-flucytosine and the resistant strains all contained S29L mutation. Isolates of all other genotypes contained wild-type codon 29 in cytosine deaminase. A simple, PCR-RFLP-based method has been developed to facilitate rapid detection of S29L mutation in cytosine deaminase. A noteworthy observation of our study is the identification of five new genotypes of C. dubliniensis isolates, recovered from oral/respiratory specimens from patients of Middle Eastern origin. Furthermore, all 5-flucytosine resistant C. dubliniensis isolates in Kuwait belonged to genotype 4 only.

Forthcoming Conferences and Meetings

Compiled and edited by
Babichan K Chandy

Kuwait Medical Journal 2012; 44 (2): 159 - 169

Family Medicine: **Dermatology** Review
Jun 16 - 23, 2012
Holland America's ms Westerdam, Seattle, WA, *United States*
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

9th National Neuroscience Conference: **Epilepsy in Children** 2012
Jun 20, 2012
Hallam Conference Centre, London, *United Kingdom*
Contact: Rikki Bhachu, St Judes Church, Dulwich Road, London, SE24 0PB
Tel: 020 7501 6734 Fax: 020 7978 8319
Email: rikki.bhachu@markallengroup.com

Cardiomyocyte Regeneration and Protection
Jun 20 - 21, 2011
Hilton Torrey Pines, La Jolla, CA, *United States*
Contact: Katie, Abcam, 1 Kendall Sq., Suite 341, Cambridge, MA 02139
Tel: 6175774263
Email: ks@abcam.com

12th Congress of the European Society of **Contraception and Reproductive Health**
Jun 20 - 23, 2012
Athens, *Greece*
Contact: Nancy Habils, Opalfeneweg 3, 1740 Ternat, Belgium
Tel: +32 2 582 08 52; Fax: +32 2 582 55 15
Email: congress@contraception-esc.com

13th National Conference: **Parkinson's 2011**: recent advances in clinical managament
Jun 21, 2011
CBI Conference Centre, London, *United Kingdom*
Contact: Florence Doel, St Judes Church, Dulwich Road, Herne Hill, London SE24 0PB
Tel: +44 (0) 207 501 6762; Fax: +44 (0) 207 978 8319
Email: flo.doel@markallengroup.com

Vascular Liver Diseases Conference
Jun 22 - 23, 2012
Swissôtel Tallinn, Estonia, Tallinn, *Estonia*
Contact: Kenes International, 1-3 rue de Chantepoulet P.O. Box 1726 CH-1211 Geneva, Switzerland
Tel: +41 22 908 0488; Fax: +41 22 906 9140
Email: tallinn2012@easl.eu

1st **Gynecological Surgery** Conference 2011
Jun 23 - 25, 2011
Kellogg Conference Hotel at Gallaudet University, Washington D.C, *United States*
Contact: Romy Meuter, 953 National Road, PMB#110, Wheeling, VW, 26003, USA
Tel: 1-800-662-0183; Fax: 1-800-662-0183
Email: romy@medineo.org

Family Medicine: A Review and Update of Common Clinical Problems
Jun 25 - 29, 2012
Hyatt Regency, Sarasota, FL, *United States*
Contact: D. Reece Pierce, PA-C, P.O. Box 49947
Tel: 866-267-4263; Fax: 941-365-7073
Email: mail@ams4cme.com

Atrial Fibrillation
Jun 26, 2012
London, *United Kingdom*
Contact: Heather Ikwuemesi, St Jude's church
Tel: 02075016760
Email: heather.ikwuemesi@markallengroup.com

Family Medicine
Jun 30 - Jul 7, 2012
Royal Caribbean's Oasis of the Seas, Ft. Lauderdale, FL, *United States*
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.ne

Novel treatments for **Schizophrenia**: Prevention and cognitive remediation
Jul 4, 2012
New York, NY, *United States*
Contact: Columbia University CME, 601 West 168th Street, Suite 51, New York, NY
Tele: 212-305-3334; Fax: 212-781-6047
Email: cme@columbia.edu

10th national conference: **Autism** Today: Summer Meeting
Jul 5 - 6, 2012
Cavendish Conference Centre, London, *United Kingdom*
Contact: Florence Doel, St Judes Church, Dulwich Road, London, SE24 0PB
Te: +44 (0)207 501 6762 Fax: +44 (0)207 978 8319
Email: flo.doel@markallengroup.com

British **Gynaecological Cancer** Society Annual Meeting
Jul 5 - 6, 2012
The QEII Conference Centre, London, *United Kingdom*
Contact: Kenes UK, 1st Floor, Chesterfield House 385 Euston Road London, NW1 3AU United Kingdom
Tel: +44 (0) 20 7383 8030
Email: bgcs@kenes.com

A Cute Perspective on **Chronic Disease Management** (Pre Conference Cruise)
Jul 6 - 14, 2012
Copenhagen, *Denmark*
Contact: Mathew Lazarow , Senior Account Manager, Amaco Travel and Conference
Tel: 011-61-3-9535-3666; Fax: 011-61-3-9561-4507
Email: mathew.lazarow@amacotravel.com.au

ESPU Sponsored Course : Laparoscopic Course of **Pediatric Urology**
Jul 6 - 7, 2012
Naples, *Italy*
Contact: Prof. Ciro Esposito, Pediatric Surgery, University of Naples
Tel: 011-39-81-746-3378; Fax: 011-39-81-746-3361
Email: ciroespo@unina.it

Infectious Disease Review
Jul 7 - 14, 2012
Holland America's ms Westerdam, Seattle, WA, *United States*
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

Primary Care Update: **Type 2 Diabetes, Metabolic Syndrome and Obesity**
Jul 7 - 17, 2012
Holland America's ms Noordam, Civitavecchia, *Italy*
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

Immunoreceptors
Jul 8 - 13, 2012
Snowmass; Colorado, *United States*
Contact: Federation of American Societies for Experimental Biology
Tel: 301-634-7000; Fax: 301-634-7001
Email: info@faseb.org

Growth Hormone/Prolactin Family in Biology & Disease
Jul 8 - 13, 2012
Snowmass; Colorado, *United States*
Contact: Federation of American Societies for Experimental Biology
Tel: 301-634-7000; Fax: 301-634-7001
Email: info@faseb.org

ECNP School of **Neuropsychopharmacology**
Jul 8 - 13, 2012
Oxford, *United Kingdom*
Contact: European College of Neuropsychopharmacology
Tel: 011-31-30-253-8567; Fax: 011-31-30-253-8568
Email: ecnpschool@ecnp.eu

6th Baltic Sea Summer School on **Epilepsy**
Jul 8 - 13, 2012
Rostock; *Germany*
Contact: Petra Novotny , BSSSE Office
Email: petra.novotny@wolfstiftung.org

Psychiatry Review Disney Alaska Cruise
Jul 9 -16, 2012
Seattle, Washington, *United States*
Contact: Lystra Singh , Conference Coordinator
Tel: 647-882-1427
Email: info@psychiatryreviewcourse.com

ICAO 2012, 3rd International Congress on **Abdominal Obesity**
Jul 9 - 12, 2012
Québec Congress Center, Quebec City, *Canada*
Contact: Kenes International, 1-3 Rue de Chantepoulet, PO Box 1726, CH-1211, Geneva 1, Switzerland
Tel: + 41 22 908 0488; Fax: + 41 22 906 9140
Email: icao@kenes.com

British Society for **Allergy and Clinical Immunology**
Jul 11 - 13, 2012
East Midlands Conference Centre University Park Nottingham NG7 2RJ, Nottingham, *United Kingdom*
Contact: Kenes UK, 1st Floor, Chesterfield House 385 Euston Road London, NW1 3AU United Kingdom
Tel: +44 (0) 20 7383 8030
Email: bsaci@kenes.com

Regulation of **Adult Neurogenesis**: from Epigenetics to Behavior
Jul 12 - 13
Barcelona, *Spain*
Contact: , Abcam Events Team
Tel: 011-44-12-2369-6000
Email: events@abcam.com

Practical Ways to Achieve Targets in **Diabetes Care**
Jul 12 – 15, 2012
Keystone / Colorado, *United States*
Contact: Marijane Engel , Children's Diabetes Foundation
Tel: 800-695-2873 or 303-863-1200; Fax: 303-863-1122
Email: mj@childrensdiabetesfoundation.org

Facial Plastic Surgery Flap Reconstruction Dissection Course
Jul 12, 2012
Dundee, *United Kingdom*
Contact: Susan McComiskie , Secretary , Cuschieri Skills Centre, University of Dundee
Tel: 011-44-13-8264-5857; Fax: 011-44-13-8264-6042
Email: s.mccomiskie@dundee.ac.uk

Animation Therapy: Introducing an Innovative Therapeutic Tool in Clinical Practice
American Orthopaedic Society for Sports Medicine 2012 Annual Meeting
Jul 12 - 15, 2012
Baltimore, *Maryland*
Contact: American Orthopaedic Society for Sports Medicine
Tel: 847-292-4900
Email: aossm@aossm.org

3rd **Critical Care** Conference in Thailand 2012
Jul 12 - 14, 2012
Bangkok, *Thailand*
Contact: Asaya Rattanahol , Miss , WB Organizer
Tel: 011-66-2-714-2590; Fax: 011-66-2-714-2656
Email: tsccmconference@gmail.com

Society of Dermatology Physician Assistants (SDPA) Annual Summer **Dermatology** Conference
Jul 12 - 15, 2012
Seattle, Washington, *United States*
Contact: Rose Hawker, SDPA
Tel: 830-980-8489
Email: conferences@dermpa.org

Trauma Care Course
Jul 12- 13, 2012
Denver / Colorado, *United States*
Contact: Evelyn Smith , Denver Health
Tel: 303-602-2703
Email: Evelyn.Smith@dhha.org

19th ASEAN Federation of **Cardiology** Congress 2012
Jul 13 - 15, 2012
Raffles City Convention Centre, *Singapore*
Contact: Kelly Chan , The Meeting Lab Pte Ltd
Tel: 011-65-6346-4402; Fax: 011-65-6346-4403
Email: kellychan@themeetinglab.com

Primary Care: **Allergy and Immunology** Alaska Cruise
Jul 13 - 20, 2012
Vancouver / British Columbia , *United States*
Contact: Reservations , Meeting Planner , Continuing Education, Inc.
Tel: 800-422-0711 or 727-526-1571; Fax: 727-522-8304
Email: contactus@continuingeducation.net

8th FENS Forum of **Neuroscience**
Jul 14 - 18, 2012
Barcelona, *Switzerland*
Contact: Kenes International, 1-3, Rue de Chantepoulet, France
Tel: 4122908048; Fax: 4122906914
Email: fens@kenes.com

Dermatology for the PCP
Jul 14- 24, 2012
Holland America's ms Eurodam, Copenhagen, *Denmark*
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

Phospholipid Metabolism: Disease, Signal Transduction, & Membrane Dynamics
Jul 15 - 20, 2012
Saxtons River / Vermont, *United States*
Contact: , Federation of American Societies for Experimental Biology
Tel: 301-634-7000; Fax: 301-634-7001
Email: info@faseb.org

Analysis & Reporting of the **Adult Echocardiogram**: The Essential Foundation
Jul 19 - 20, 2012
Texas / Dallas, *United States*
Contact: Amy Donaldson , Administrator , Keith Mauney & Associates Ultrasound Training Institutes
Tel: 800-845-3484 or 972-353-3200; Fax: 817-577-4200
Email: info@kmaultrasound.com

BC3 **Breast Cancer** Coordinated Care Conference
Jul 19 - 21, 2012
District of Columbia / Washington, *United States*
Contact: Dennis A. Vitrella , Conference Director , International Conference Management
Tel: 337-235-6606; Fax: 337-235-7300
Email: DVitrella@BC3conference.com

Diagnostic and Interventional **Musculoskeletal Ultrasound**
Jul 19 - 21, 2012
Minnesota / Rochester (MN) , *United States*
Contact: Danielle Delanko , Mayo School of Continuous Professional Development
Tel: 800-638-5352 or 301-498-4100
Email: ddelanko@aium.org

Neurology in Clinical Practice
Jul 19 - 21, 2012
Illinois / Chicago, *United States*
Contact: Mayo School of Continuous Professional Development
Tel: 800-323-2688 (U.S.) or 507-284-2509 (outside the U.S.)
Email: cme@mayo.edu

2012 Annual Conference of Australasian College of **Skin Cancer Medicine**
Jul 20 - 22, 2012
Gold Coast, *Australia*
Contact: Australasian College of Skin Cancer Medicine
Tel: 011-61-4-1491-0355; Fax: 011-61-7-3273-1903
Email: enq@skincancercollege.com

34th Annual **Pediatric Primary Care** Conference
Jul 20 - 22, 2012
Virginia / Virginia Beach Family Medicine, *United States*
Contact: Carole Hettema , Medical College of Virginia
Tel: 804-828-3640
Email: chettema@mcvh-vcu.edu

20th World Congress of the International Association for **Child & Adolescent Psychiatry**
Jul 21 - 25, 2012
Paris Psychiatry, *France*
Contact: Laure Machefer, Registration Manager , Colloquium Conferences
Tel: 011-33-1-4464-1465; Fax: 011-33-1-4464-1516
Email: iacapap2012@clq-group.com

Symposia at Sea: **Head & Neck** Imaging
Jul 21 – 28, 2012
Italy
Contact: Educational Symposia
Tel: 800-338-5901 or 813-806-1000; Fax: 813-806-1001
Email: info@edusymp.com

Visiting Fellowship in **Transcranial Magnetic Stimulation**
Jul 21 - 22, 2012
North Carolina / Durham Neurology, *United States*
Contact: Office of Continuing Medical Education, Duke University School of Medicine
Tel: 919-401-1200; Fax: 919-401-1213
Email: cme@mc.duke.edu

8th International Conference on **Head and Neck Cancer**
Jul 21 - 25, 2012
Metro Toronto Convention Center (South Building), Toronto, *Canada*
Contact: Jennifer Clark, 11300 W. Olympic Blvd, Suite 600, Toronto, CA
Tel: 310-437-0559
Email: jennifer@ahns.info

Geriatric Medicine Review
Jul 21 - 28, 2012
Holland America's ms Westerdam, Seattle, WA, *United States*
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

Primary Care: **Mental Health** Issues with a Focus on Drugs and Behavior
Jul 21 - 28, 2012
Royal Caribbean Splendour of the Seas, Venice, *Italy*
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

30th International Congress of **Psychology** - ICP 2012
Jul 22 - 27, 2012
Cape Town International Convention Centre, Cape Town, *South Africa*
Contact: Fatima Seedat, PO Box 989, Houghton 2041, South Africa
Tel: 011 486 3322; Fax: 011 486 3266
Email: info@icp2012.com

Tyrosine Kinase Signaling in Cancer, Disease, & Development
Jul 22 – 27, 2012
Colorado / Snowmass, *United States*
Contact: Federation of American Societies for Experimental Biology
Tel: 301-634-7000; Fax: 301-634-7001
Email: info@faseb.org

Neurotrauma 2012
Jul 22 - 25, 2012
Arizona, *United States*
Contact: Karen Gottlieb, CMP, President, TLC Events Group, Inc.
Tel: 305-661-5581
Email: nns@neurotrauma.org

Lung Epithelium in Health & Disease
Jul 22 - 27, 2012
Vermont / Saxtons River, *United States*
Contact: Federation of American Societies for Experimental Biology
Tel: 301-634-7000; Fax: 301-634-7001
Email: info@faseb.org

Lipid Droplets: Metabolic Consequences of the Storage of Neutral Lipids
Jul 22 - 27, 2012
Colorado / Snowmass, *United States*
Contact: Federation of American Societies for Experimental Biology
Tel: 301-634-7000; Fax: 301-634-7001
Email: info@faseb.org

19th International **AIDS** Conference
Jul 22 - 27, 2012
District of Columbia, *United States*
Contact: Conference Secretariat
Tel: 011-41-22-710-0800
Email: info@aids2012.org

10 Day Seminar on the **Epidemiology & Prevention of Cardiovascular Disease** 2012
Jul 22 - 3, 2012
California, *United States*
Contact: American Heart Association
Tel: 888-242-2453 or 214-570-5935; Fax: 214-373-3406
Email: scientificconferences@heart.org

Medical **CBT (Cognitive Behavior Therapy) for Depression**: Ten-Minute Techniques for Real Doctors
Jul 23 - 25, 2012
British Columbia, *Canada*
Contact: Greg Dubord, MD , CME Director , CBT Canada
Tel: 877-466-8228
Email: registrar@cbt.ca

Autism, ADHD & Other Pediatric Behavior Disorders
Eastern Mediterranean Cruise
Jul 23 - Aug 3,2012
Rome, *Italy*
Contact: Continuing Education, Inc.
Tel: 800-422-0711 or 727-526-1571

11th Asia Pacific Congress on **Deafness**
Jul 26 - 28, 2012
Singapore, *Singapore*
Contact: Ms. Marianne Yee , Congress Secretariat , National University Hospital Singapore
Tel: 011-65-6410-9698
Email: secretariat@apcd2012.com

15th Annual **Osteoporosis** Conference
Jul 26 - 28, 2012
South Carolina, *Kiawah Island*
Contact: Vicki Baugh, Coordinator , Southern Medical Association
Tel: 800-423-4992; Fax: 205-945-1548
Email: vickib@sma.org

Metabolic and Endocrine Disease Summit MEDS East
Jul 26 - 28, 2012
Disney World Endocrinology, Florida,*United States*
Contact: Kim Kirchner , Registration Coordinator , Quadrant HealthCom
Tel: 502-574-9023; Fax: 502-589-3602
Email: kkirchner@hqtrs.com

Pediatric & Adult Infectious Diseases: An Evidence-Based Approach to Common Problems
Jul 26 - 28, 2012
Wisconsin Dells, Wisconsin, *United States*
Contact: Orly Light , Director , MCE Conferences
Tel: 888-533-9031; Fax: 858-777-5588
Email: info@mceconferences.com

Nuclear Cardiology Board Exam Preparation Course
Jul 27 - 29, 2012
Chicago, Illinois, *United States*
Contact: American Society of Nuclear Cardiology
Tel: 301-215-7575; Fax: 301-215-7113
Email: info@asnc.org

Retinal Neurobiology & Visual Processing
Jul 29 - Aug 3, 2012
Steamboat Springs, Colorado, *United States*
Contact: Federation of American Societies for Experimental Biology
Tel: 301-634-7000; Fax: 301-634-7001
Email: info@faseb.org

Hands-On **Peripheral Vascular Ultrasound Imaging**
Jul 30 - Aug 1, 2012
Dallas/Texas, *United States*
Contact: Amy Donaldson , Administrator , Keith Mauney & Associates Ultrasound Training Institutes
Tel: 800-845-3484 or 972-353-3200; Fax: 817-577-4200
Email: info@kmaultrasound.com

Integration of **Genomic & Non-Genomic Steroid Receptor Actions**
Jul 29 - Aug 3, 2012
Snowmass/Colorado, *United States*
Contact: Federation of American Societies for Experimental Biology
Tel: 301-634-7000; Fax: 301-634-7001
Email: info@faseb.org

Improving **Pain Management** in Primary Care
Jul 30 - Aug 1, 2012
Anaheim / California, *United States*
Contact: Orly Light, Director , MCE Conferences
Tel: 888-533-9031; Fax: 858-777-5588
Email: info@mceconferences.com

37th Annual Aspen Psychiatry Conference Enhanced Treatment, Better Outcomes: **Depression, Anxiety, Stress**
Aug 1 - 3, 2012
Aspen / Colorado, *United States*
Contact: Lesley Lundeen, Program Coordinator, University of Colorado Denver
Tel: 303-724-7401
Email: Lesley.Lundeen@ucdenver.edu

9th Annual EUS & Principles and Pearls in **Pancreatology**
Aug 1 - 4, 2012
Rochester / (MN)Minnesota, *United States*
Contact: Mayo School of Continuous Professional Development
Tel: 800-323-2688
Email: cme@mayo.edu

Medical **Cognitive Behaviour Therapy**
Aug 1 - 8, 2012
Turks/Caicos / Grace Bay, *United States*
Contact: CBT (Cognitive Behavior Therapy) Canada
Tel: 877-466-8228
Email: info@cbt.ca

Renal Biopsy in Medical Diseases of the Kidneys
Aug 1 - 4, 2012
New York, *United States*
Contact: Continuing Medical Education, Columbia University
Tel: 212-305-3334; Fax: 212-781-6047
Email: cme@columbia.edu

Hands-On **Carotid & Vertebral Duplex Ultrasound Imaging**
Aug 2 - 3, 2012
Dallas / Texas, *United States*
Contact: Amy Donaldson, Administrator, Keith Mauney & Associates Ultrasound Training Institutes
Tel: 800-845-3484 or 972-353-3200; Fax: 817-577-4200
Email: info@kmaultrasound.com

Advanced **Cardiovascular Solutions (ACVS)** India 2012
Aug 3 - 5, 2012
Hyderabad, *India*
Contact: Susheel Kodali, MD , Director, Interventional Cardiology Fellowship Program , Columbia University Medical Center
Tel: 212-305-7060; Fax: 212-342-3660
Email: acvshi@gmail.com

Mitosis: Spindle Assembly & Function
Aug 5 - 10, 2012
Steamboat Springs / Colorado, *United States*
Contact: Federation of American Societies for Experimental Biology
Tel: 301-634-7000; Fax: 301-634-7001
Email: info@faseb.org

COGNO 5th Annual Scientific Meeting - **Neuroimaging**: Novel Approaches for Glioma
Aug 7 - 9, 2012
Brisbane, *Australia*
Contact: Cooperative Trials Group for Neuro-Oncology
Email: cogno@ctc.usyd.edu.au

Evidence Based Treatment of Heart Failure, **Anticoagulation & Pain Management**
Aug 8 - 10, 2012
Colorado Springs / Colorado, *United States*
Contact: Stephanie Naski , Marketing Manager , University Learning Systems
Tel: 800-940-5860; Fax: 716-529-0550
Email: stephanie.naski@universitylearning.com

Bone Densitometry Course
Aug 8 - 9, 2012
Crowne Plaza Albuquerque, Albuquerque, NM, *United States*
Contact: Amy Scrivens, 306 Industrial Park Road Suite 206, Middletown, CT 06457
Tel: 860-259-1000; Fax: 860-259-1030
Email: ascrivens@iscd.org

Difficult Airway Course: EMS
Aug 11 - 12, 2012
Bristol, VA, *United States*
Contact: The Difficult Airway Course
Tel: 336-880-4552; Fax: 336-869-6026
Email: mskarote@theairwaysite.com

Skeletal Muscle Satellite & Stem Cells
Aug 12 - 17, 2012
Barga Biochemistry, *Italy*
Contact: Federation of American Societies for Experimental Biology
Tel: 301-634-7000; Fax: 301-634-7001
Email: info@faseb.org

8th World Congress on Active Ageing
Aug 13 -17, 2012
Glasgow, *United Kingdom*
Contact: Congrex UK
Tel: 011-44-14-1331-0123; Fax: 011-44-14-1331-0234
Email: info@wcaa2012.com

Intensive Review of **Gastroenterology & Hepatology**: Board Oriented Certification & Recertification
Aug 15 - 18, 2012
San Diego / California, *United States*
Contact: Cleveland Clinic
Tel: 800-238-6750 or 216-448-0770
Email: cmeregistration@ccf.org

Vascular Ultrasound Analysis and Report Formulation
Aug 15 - 16, 2012
Dallas / Texas, *United States*
Contact: Amy Donaldson, Administrator, Keith Mauney & Associates Ultrasound Training Institutes
Tel: 800-845-3484 or 972-353-3200; Fax: 817-577-4200
Email: info@kmaultrasound.com

Infectious Disease Medicine for Primary Care Physicians
Aug 17 - 19, 2012
Lake George / New York, *United States*
Contact: Medical Education Resources
Tel: 303-798-9682; Fax: 303-798-5731
Website: http://mer.org/

21st World Congress of **Asthma**
Aug 18 - 21, 2012
Quebec City / Quebec, *Canada*
Contact: Niki Gargassoula , President & M. Director , Frei S.A. Travel-Congress
Tel: 011-30-210-321-5600; Fax: 011-30-210-321-9296
Email: wca-2012@frei.gr

The 30th World Congress of **Biomedical Laboratory** Science
Aug 18 - 22, 2012
Maritim proArte Hotel, Berlin, *Germany*
Contact: Ilana Berkowitz, 18 Avenue Louis-Casai, 1209 Geneva, Switzerland
Tel: 41 22 5330 948; Fax: 41 22 5802 953
Email: secretariat@ifbls-dvta2012.com

11th Asian Congress of **Urology**
Aug 22 - 26, 2012
Pataya, *Thailand*
Contact: Congress Secretariat , Convention Organisers Co., Ltd.
Tel: 011-66-2-287-3942/3488; Fax: 011-66-2-677-5868
Email: secretariat@11thacu2012.org

6th Annual Joint Course: New Technology for the Treatment of **Adult Hip & Knee Disorders**
Aug 23 - 25, 2012
Baltimore \ Maryland, *United States*
Contact: Madeline Bacon , Manager of Academic and Research Programs , Rubin Institute for Advanced Orthopedics/Sinai Hospital of Baltimore
Tel: 410-601-9798; Fax: 410-601-0585
Email: mbacon@lifebridgehealth.org

Pediatrics Review
Aug 25 - Sep 1, 2012
Holland America's ms Westerdam, Seattle, WA, *United States*
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

Psychiatry in Medical Settings
Aug 26 - 28, 2012
JW Marriott Desert Ridge Resort, Phoenix, AZ, *United States*
Contact: MSCPD, 200 1st Street /Rochester, MN 55905
Tel: 800-323-2688; Fax: 507-284-0532
Email: hovey.sierra@mayo.edu

Clinical Practice & Implementation of I**mage-Guided Stereotactic Body Radiotherapy**
Sep 2 - 6, 2012
Würzburg, *Germany*
Contact: European Society for Radiotherapy & Oncology
Tel: 011-32-2-775-9340; Fax: 011-32-2-779-5494
Email: education@estro.org

4th International Course in Nutritional Epidemiology
Sep 3 - 14, 2012
London, *United Kingdom*
Contact: Nikki Whitelock , Course Administrator , School of Public Health, Imperial College
Tel: 011-44-20-7594-2116
Email: nutrition-epi-course@imperial.ac.uk

14th European **Symposium of Suiside & Suicidal Behaviour**
Sep 3 - 6, 2012
Tel Aviv - Jaffa, *Switzerland*
Contact: Kenes, 1-3, Rue de Chantepoulet,
Tel: 4122908048; Fax: 4122906914
Email: esssb@kenes.com

30th World Congress of **Endourology and SWL**
Sep 4 - 8, 2012
Istanbul, *Turkey*
Contact: Congress Organizing Secretariat , Topkon Congress Services
Tel: 011-90-216-330-9020; Fax: 011-90-216-330-9005
Email: wce2012@topkon.com

Hands-on **Cardiac Morphology**
Sep 5 - 7, 2012
London, *United Kingdom*
Contact: ICH Events
Tel: 011-44-20-7905-2699 / 2675; Fax: 011-44-20-7831-6902
Email: info@ichevents.com

The 8th International Conference on **Frontotemporal Dementias**
Sep 5 - 7, 2012
Manchester, *United Kingdom*
Contact: Kenes UK, 385 Euston Road
Tel: 44 (0) 20 7383 8030; Fax: 44 (0) 20 7383 8040
Email: ftd@kenes.com

Arrhythmias in the Real World 2012
Sep 6 - 8, 2012
Washington, District of Columbia, *United States*
Contact: American College of Cardiology Foundation
Tel: 800-253-4636 ext. 5603 or 202-375-5000; Fax: 202-375-7000
Email: resource@acc.org

The **Viral Hepatitis** Congress
Sep 7 - 9, 2012
Johann Wolfgang Goethe-Universität, Frankfurt, *Germany*
Contact: Michele Upton, Victoria Mill, Windmill Street, Macclesfield, Cheshire, SK11 7HQ, UK
Tel: +44 (0) 1625 664195
Email: hep@kp360group.com

Bone Densitometry Course
Sep 8 - 9, 2012
St. Louis Airport Marriott, St. Louis, MO, *United States*
Contact: Amy Scrivens, 306 Industrial Park Road Suite 206, Middletown, CT 06457
Tel: 860-259-1000; Fax: 860-259-1030
Email: ascrivens@iscd.org

24th European Congress of Pathology
Sep 8 - 12, 2012
Prague Congress Centre, Prague, *Czech Republic*
Contact: Juliane Heinicke, Paulsborner Str. 44
Tel:+49 – 30 – 300 669-0 Fax: +49 – 30 – 305 73 91
Email: ecp-prague@cpo-hanser.de

Advances in **Rheumatology**
Sep 8 - 11 , 2012
Boston / Massachusetts, *United States*
Contact: Department of Continuing Education , Harvard Medical School
Tel: 617-384-8600
Email: hms-cme@hms.harvard.edu

New Advances in **Inflammatory Disease**
Sep 8 - 9, 2012
San Diego / California , *United States*
Contact: Scripps Conference Services & CME
Tel: 858-652-5400; Fax: 858-652-5565
Website: http://www.scripps.org/health-education

Hands-On Obstetric & Pelvic Ultrasound Imaging
Sep 10 - 13, 2012
Dallas /Texas , *United States*
Contact: Amy Donaldson, Administrator , Keith Mauney & Associates Ultrasound Training Institutes
Tel: 800-845-3484 or 972-353-3200; Fax: 817-577-4200
Email: info@kmaultrasound.com

One-day Update in **Thrombosis & Haemostasis** for Consultants & Advanced SpRs
Sep 11, 2012
London, *United Kingdom*
Contact: , St. Mary's, Imperial College
Tel: 011-44-20-7589-5111
Email: haemsec@imperial.ac.uk

The American Society of Emergency Radiology 2012 Annual Meeting and Postgraduate Course in **Trauma and Emergency Radiology**
Sep 12 - 15, 2012
New Orleans Marriott, New Orleans, LA, *United States*
Contact: Savanna Lott, 4550 Post Oak Place, Suite 342
Tel: 713-965-0566
Email: aser@meetingmanagers.com

Hands-On **Carotid & Vertebral Duplex Ultrasound Imaging**
Sep 13 - 14 , 2012
Dallas / Texas , *United States*
Contact: Amy Donaldson , Administrator , Keith Mauney & Associates Ultrasound Training Institutes
Tel: 800-845-3484 or 972-353-3200; Fax: 817-577-4200
Email: info@kmaultrasound.com

Inherited Kidney Disorders: An Update
Sep 13 - 1, 2012
Toulouse, *France*
Contact: Prof. Dominique Chauveau , Service de Néphrologie, Hôpital de Rangueil
Tel: 011-33-5-6132-3279
Email: chauveau.d@chu-toulouse.fr

6th Annual Conference of International **Liver Cancer** Association (ILCA)
Sep 14 - 16, 2012
Bwerlin, *Germany*
Contact: Céline Nieuwenhuys , Conference Manager , ILCA Office
Tel: 011-32-2-789-2345; Fax: 011-32-2-743-1550
Email: info@ilca-online.org

Orthopaedics and Sports Medicine Bermuda Cruise
Sep 14 - 21, 2012
Boston, Massachusetts, *United States*
Contact: Reservations, Meeting Planner, Continuing Education, Inc.
Tel: 800-422-0711 or 727-526-1571; Fax: 727-522-8304
Email: contactus@continuingeducation.net

Perspectives in **Melanoma 16**
Sep 14 - 15, 2012
Valencia, *Spain*
Contact: , Imedex
Tel: 770-751-7332; Fax: 770-751-7334
Email: meetings@imedex.com

Wound Care
Sep 15 - 22, 2012
Royal Caribbean's Oasis of the Seas, Ft. Lauderdale, FL, *United States*
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

Developmental Behavioral Pediatrics Symposium
Sep 17, 2012
Riyadh, *Saudi Arabia*
Contact: Ms Jaina Abdulkadil , Continuous Professional Development , King Fahad Medical City
Tel: 011-966-1–288–9999 ext. 7497; Fax: 011-966-1–288–9000 ext. 4114
Email: cme@kfmc.med.sa

Medical Ethics
Sep 17 - 21, 2012
London, *United Kingdom*
Contact: Continuing Professional Development, Imperial College London
Tel: 011-44-20-7594-6881; Fax: 011-44-20-7594-6883
Email: cpd@imperial.ac.uk

Recent Advances in **Nuclear Medicine**
Sep 18 - 19, 2012
Vinnitsa, *Ukraine*
Contact: Kristina Zadorina, Nbscience
Tel: 011-38-4-4233-2770
Email: ukraine@nbscience.com

2nd International Conference on **Regenerative Orthopaedics & Tissue Engineering**
Sep 20 - 22, 2012
Opatija, *Croatia*
Contact: Svjetlana Vukic, Depol komunikacije d.o.o.
Tel: 011-385-1-244-4333; Fax: 011-385-1-243-1478
Email: svjetlana@depol.org

Medical Cognitive Behavior Therapy for Depression: Ten-Minute Techniques for Real Doctors
Sep 20 - 21, 2012
Vancouver, British Columbia, *Canada*
Contact: Greg Dubord, MD, CME Director, CBT Canada
Tel: 877-466-8228
Email: registrar@cbt.ca

Virtual Colonoscopy Workshop
Sep 20 - 22, 2012
San Francisco, California, *United States*
Contact: UCSF CME Registration Office
Tel: 415-476-5808; Fax: 415-502-1795
Email: info@ocme.ucsf.edu

Carotid & Transcranial Doppler
Sep 21 - 23, 2012
Las Vegas/Nevada, *United States*
Contact: Institute for Advanced Medical Education
Tel: 802-824-4433
Website: https://iame.com/conferences/

Masters of **Mininmally Invasive Thoracic Surgery**
Sep 21 - 22, 2012
New York, *United States*
Contact: Office of Continuing Medical Education, Duke University School of Medicine
Tel: 919-401-1200; Fax: 919-401-1213
Email: cme@mc.duke.edu

5th International **Hemodialysis** Course
Sep 24 - 28, 2012
Mansoura, *Egypt*
Contact: Hussein Sheashaa
Email: sheashaa@mans.edu.eg

Musculoskeletal (the comprehensive course)
Sep 24 - 28, 2012
Valencia, *Spain*
Contact: Maria Jose Garcia, Technical Secretary, Fundación Universidad-Empresa, ADEIT
Tel: 011-34-96-205-7925; Fax: 011-34-96-326-2700
Email: maria.jose.garcia@adeit.uv.es

Advanced Brain Imaging: Beyond State-of-the-Art
Sep 27 - 302, 2012
McLean Internal Medicine, Neurology, Radiology/Imaging , *Virginia*
Contact: Melisa Martinez, Meetings Coordinator, ISMRM
Tel: 510-841-1899; Fax: 510-841-2340
Email: info@ismrm.org

Ambulatory OB/GYN Nursing
Sep 27 - 29, 2012
Boston / Massachusetts, *United States*
Contact: Contemporary Forums
Tel: 800-377-7707; Fax: 800-329-9923
Email: info@cforums.com

Ultrasound and Maternal-Fetal Medicine Course
Sep 28 - 29, 2012
Granada, *Spain*
Contact: Ana Maria Diaz Chaves , Facultad de Medicina | Universidad de Granada
Tel: 011-34-958-24-2867
Email: anamdiaz@ugr.es

27th Annual Critical Issues in **Tumor Microenvironment, Angiogenesis & Metastastasis**
Oct 1 - 4, 2012
Cambridge, Massachusetts, *United States*
Contact: Department of Continuing Education , Harvard Medical School
Tel: 617-384-8600; Fax: 617-384-8686
Email: hms-cme@hms.harvard.edu

Brain Injuries
Oct 3 - 6, 2012
Las Vegas / Nevada, *United States*
Contact: Contemporary Forums
Tel: 800-377-7707; Fax: 800-329-9923
Email: info@cforums.com

Riding the Wave: Advances in the Treatment & Research of **Inherited Neuromuscular Conditions**
Oct 4 - 7, 2012
Gold Coast, *Australia*
Contact: Deborah Robins, Duchenne Foundation
Tel: 011-61-7-4057-5731
Email: deborah.robins@duchennefoundation.org.au

6th Asian Congress of **Paediatric Infectious Diseases**
Oct 24 - 27, 2012
Bandaranaike Memorial International Conference Hall, Bauddhaloka Mawatha, *Sri Lanka*
Contact: Kenes Asia, ACPID 2012 Conference Secretariat Kenes Asia 5th Floor, PICO Creative Centre 20 Kallang Avenue, Singapore 339411
Tel: +65 6292 0723; Fax: +65 6292 4721
Email: acpid2012@kenes.com

Infectious Disease Review
Nov 10 - 17, 2012
Norwegian Cruise Line's Pride of America, Honolulu, HI, *United States*
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

11th International Congress on **Drug Therapy in HIV Infection**
Nov 11 - 15, 2012
SECC, Glasgow, *United Kingdom*
Contact: Mandy Shore, Victoria Mill, Windmill Street, Macclesfield, Cheshire SK11 7HQ, UK
Tel: +44 (0)1625 664390; Fax +44 (0)1625 664391
Email: HIV11@kp360group.com

XXXI World Congress of **Internal Medicine**
Nov 11 - 15, 2012
Espacio Riesco, Santiago, *Switzerland*
Contact: Kenes, La Concepción 266 Office 501, Santiago, Chile
Tel: 56-2-9462633; Fax: 56-2-946 2643
Email: wcim2012@kenes.com

The 2nd International **Multidisciplinary Forum on Palliative Care**
Nov 24 - 25, 2012
Hilton Florence Metropole, Hilton Florence Metropole, *Italy*
Contact: Meital Fridenzon, 18 Avenue Louis-Casai | 1209 Geneva | Switzerland
Tel: 41 22 5330 948; Fax: 41 22 5802 953
Email: mfridenzon@paragon-conventions.com

Hands-on Ultrasound-Guided **Peripheral Nerve Blocks**
Dec 1 - 2, 2012
Anesthesiology, Iowa City, *Iowa*
Contact: , Regional Anesthesia Study Center of Iowa , University of Iowa Health Care
Tel: 319-384-9273; Fax: 319-356-2940
Email: rasci@uiowa.edu

1st American **Diabetes** Association Middle East Congress
Dec 4 - 6 , 2012
Dubai, *United Arab Emirates*
Contact: Mohamed Nagd , Marketing Executive , Pure Spot Congress and Event Organizers
Tel: 011-20-2-2672-1944; Fax: 011-20-2-2671-8421
Email: info@EGYPURE.org

10th Asia-Pacific Conference on **Human Genetics** 2012
Dec 5 - 8, 2012
Kuala Lumpur, *Malaysia*
Contact: Ms Marcus Chew, Congress Secretariat, Console Communication
Tel: 011-60-3-2162-0566; Fax: 011-60-3-2161-6560
Email: info@apchg2012.org

22nd World Congress of International Association of **Surgeons, Gastroenterologists & Oncologists**
Dec 5 - 8, 2012
Bangkok,*Thailand*
Contact: Kenes InternationalMedia and Advertising, Kenes International
Tel: 011-66-2-748-7881
Email: info@iasgo2011.org

The 22nd World Congress of the International Association of Surgeons, **Gastroenterologists and Oncologists**
Dec 5 - 8, 2012
Shangri-La Hotel – Bangkok, Bangkok, *Thailand*
Contact: Kenes International, Sukhumvit Road, Bangna Bangkok, 10260 Thailand
Tel: +66 2 748 7881
Email: info@iasgo2011.org

10th Asia-Pacific Conference on **Human Genetics** 2012(10th APCHG2012)
Dec 5 - 8, 2012
Kuala Lumpur, *Malaysia*
Contact: Cristina Ang, Suite 12.9, Level 12, Wisma UOA II, 21 Jln Pinang 50450 Kuala Lumpur
Tel: 603-2162 0566; Fax: 603-2161 6560
Email: cristina@console.com.my

Advances in **Gynaecology**: Reproductive and Post-Reproductive Years
Dec 6 - 7 , 2012
London, *United Kingdom*
Contact: The Symposium Office, Imperial College London
Tel: 011-44-20-7594-2150; Fax: 011-44-20-7594-2155
Email: sympreg@imperial.ac.uk

Medical Management of **HIV/AIDS**
Dec 6 - 8, 2012
San Francisco / California, *United States*
Contact: Office of Continuing Medical Education, UCSF CME Registration Office
Tel: 415-476-5808; Fax: 415-502-1795
Email: info@ocme.ucsf.edu

World Congress of **Clinical Lipidology**
Dec 6 - 9, 2012
Budapest, *Hungary*
Contact: Vikki Hyman , Conference Manager, Paragon-Conventions
Tel: 011-41-22-533-0948; Fax: 011-41-22-580-2953
Email: vhyman@paragon-conventions.com

2nd **Pediatric Neurology** Conference 2012
Dec 8 - 10, 2012
Abu Dhabi, *United Arab Emirates*
Contact: Roshini Pradeep , Events Coordinator , Synovetics
Tel: 011-97-1-2443-4331
Email: roshini@synovetics.com

2012 Advances in Inflammatory **Bowel Diseases, Crohn's & Colitis** Foundation's Clinical & Research Conference
Dec 13 - 15, 2012
Hollywood / Florida, *United States*
Contact: Imedex
Tel: 770-751-7332; Fax: 770-751-7334
Email: meetings@imedex.com

5th International Congress **Aortic Surgery and Anesthesia** "How to do it"
Dec 14 - 15, 2012
Milan, *Italy*
Contact: San Raffaele Scientific Institute
Tel: 011-39-2-2643-3700; Fax: 011-39-2-2643-3754
Email: info@aorticsurgery.it

Molecular Medicine Conference 2012 (MMC2012): Alternative Strategies Against Cancer & Inflammation
Dec 19 - 22, 2012
Bankkok,*Thailand*
Contact: Dr. Thawornchai Limjindaporn , Division of Molecular Medicine, Department of Research & Development, Faculty of Medicine Siriraj Hospital, Mahidol University
Tel: 011-66-02-419-7000 Exten. 6666-6670
Fax: 011-66-02-418-4793
Email: limjindaporn@yahoo.com

Primary Care - Topics in **Mental Health**
Jan 5 - 12, 2013
Fort Lauderdale / Florida, *United States*
Contact: Continuing Education, Inc., Meeting Planner, Continuing Education, Inc.
Tel: 800-422-0711 or 727-526-1571; Fax: 727-522-8304
Email: contactus@continuingeducation.net

2nd ESCMID Conference on **Invasive Fungal Infections**
Jan 16 - 18, 2013
Rome, *Italy*
Contact: Marco Moschin , Conference Secretariat , ICO
Tel: 011-39-41-526-2530; Fax: 011-39-41-527-1129

Controversies and Updates in **Vascular Surgery (CACVS)** 2013
Jan 17 - 19, 2013
Paris, *France*
Contact: Michèle Caboste, divine [id]
Fax: 011-33-4-9157-1961
Email: mcaboste@divine-id.com

Cardiology, Endocrinology + Infectious Diseases: South East Asia CME Cruise
Jan 20 - Feb 3, 2013
Singapore
Contact: Sea Courses Cruises
Tel: 888-647-7327; Fax: 888-547-7337
Email: cruises@seacourses.com

MRI of the Joints
Jan 21 - 25, 2013
Ljublijana, *Slovenia*
Contact: Jana Schiro
Tel: 011-386-1-522-8530; Fax: 011-386-1-522-2497
Email: emricourse.lj@gmail.com

2nd International Conference on **Prehypertension & CardioMetabolic Syndrome**
Jan 31 - Feb 3, 2012
Barcelona, *Spain*
Contact: Sarah Krein , Conference Secretariat , Paragon Conventions
Tel: 011-41-22-533-0948; Fax: 011-41-22-580-2953
Email: secretariat@prehypertension.org

Head and Neck Imaging
Feb 4 - 8, 2012
Vienna, *Austria*
Contact: Ines Fischer
Fax: 011-43-1-40400-4898
Email: ines.fischer@meduniwien.ac.at

2013 DF Clinical Symposia - **Advances in Dermatology**
Feb 6 - 10, 2012
Naples, *Florida*
Contact: Dermatology Foundation
Tel: 847-328-2256
Fax: 847-328-0509
Email: dfgen@dermatologyfoundation.org

WHO-Facts Sheet

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Compiled and edited by
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1. MEASLES

Overview

Measles is a highly contagious, serious disease caused by a virus. In 1980, before widespread vaccination, measles caused an estimated 2.6 million deaths each year. It remains one of the leading causes of death among young children globally, despite the availability of a safe and effective vaccine. An estimated 139,300 people died from measles in 2010 – mostly children under the age of five.

Measles is caused by a virus in the paramyxovirus family. The measles virus normally grows in the cells that line the back of the throat and lungs. Measles is a human disease and is not known to occur in animals.

Accelerated immunization activities have had a major impact on reducing measles deaths. From 2001 to 2011 more than one billion children aged 9 months to 14 years who live in high risk countries were vaccinated against the disease. Global measles deaths have decreased by 74% from 535,300 in 2000 to 139,300 in 2010.

Key facts

- Measles is one of the leading causes of death among young children even though a safe and cost-effective vaccine is available.
- In 2010, there were 139,300 measles deaths globally – nearly 380 deaths every day or 15 deaths every hour.
- More than 95% of measles deaths occur in low-income countries with weak health infrastructures.
- Measles vaccination resulted in a 74% drop in measles deaths between 2000 and 2010 worldwide.
- In 2010, about 85% of the world's children received one dose of measles vaccine by their first birthday through routine health services – up from 72% in 2000.

Signs and symptoms

The first sign of measles is usually a high fever, which begins about 10 to 12 days after exposure to the virus, and lasts four to seven days. A runny nose, a cough, red and watery eyes, and small white spots inside the cheeks can develop in the initial stage. After several days, a rash erupts, usually on the face and upper neck. Over about three days, the rash spreads, eventually reaching the hands and feet. The rash lasts for five to six days, and then fades. On average, the rash occurs 14 days after exposure to the virus (within a range of seven to 18 days).

Severe measles is more likely among poorly nourished young children, especially those with insufficient vitamin A, or whose immune systems have been weakened by HIV/AIDS or other diseases.

Most measles-related deaths are caused by complications associated with the disease. Complications are more common in children under the age of five, or adults over the age of 20. The most serious complications include blindness, encephalitis (an infection that causes brain swelling), severe diarrhea and related dehydration, ear infections, or severe respiratory infections such as pneumonia. As high as 10% of measles cases result in death among populations with high levels of malnutrition and a lack of adequate health care. People who recover from measles are immune for the rest of their lives.

Who is at risk?

Unvaccinated young children are at highest risk of measles and its complications, including death. Any non-immune person (who has not been vaccinated or

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was vaccinated but did not develop immunity) can become infected.

Measles is still common in many developing countries – particularly in parts of Africa and Asia. More than 20 million people are affected by measles each year. The overwhelming majority (more than 95%) of measles deaths occur in countries with low per capita incomes and weak health infrastructures.

Measles outbreaks can be particularly deadly in countries experiencing or recovering from a natural disaster or conflict. Damage to health infrastructure and health services interrupts routine immunization, and overcrowding in residential camps greatly increases the risk of infection.

Transmission

The highly contagious virus is spread by coughing and sneezing, close personal contact or direct contact with infected nasal or throat secretions.

The virus remains active and contagious in the air or on infected surfaces for up to two hours. It can be transmitted by an infected person from four days prior to the onset of the rash to four days after the rash erupts. Measles outbreaks can result in epidemics that cause many deaths, especially among young, malnourished children. In countries where measles has been largely eliminated, cases imported from other countries remain an important source of infection.

Treatment

Severe complications from measles can be avoided though supportive care that ensures good nutrition, adequate fluid intake and treatment of dehydration with WHO-recommended oral rehydration solution. This solution replaces fluids and other essential elements that are lost through diarrhea or vomiting. Antibiotics should be prescribed to treat eye and ear infections, and pneumonia. All children in developing countries diagnosed with measles should receive two doses of vitamin A supplements, given 24 hours apart. This can help prevent eye damage and blindness. Vitamin A supplements have been shown to reduce the number of deaths from measles by 50%.

Prevention

Routine measles vaccination for children, combined with mass immunization campaigns in countries with high case and death rates, are key public health strategies to reduce global measles deaths. The measles vaccine has been in use for over 40 years. It is safe, effective and inexpensive. It costs less than one US dollar to immunize a child against measles.

The measles vaccine is often incorporated with rubella and/or mumps vaccines in countries where these illnesses are problems. It is equally effective in the single or combined form.

In 2010, about 85% of the world's children received one dose of measles vaccine by their first birthday through routine health services – up from 72% in 2000. Two doses of the vaccine are recommended to ensure immunity, as about 15% of vaccinated children fail to develop immunity from the first dose.

WHO response

The fourth Millennium Development Goal (MDG 4) aims to reduce the under-five mortality rate by two-thirds between 1990 and 2015. Recognizing the potential of measles vaccination to reduce child mortality, and given that measles vaccination coverage can be considered a marker of access to child health services, routine measles vaccination coverage has been selected as an indicator of progress towards achieving MDG 4. Overwhelming evidence demonstrates the benefit of providing universal access to measles and rubella-containing vaccines. Globally, an estimated 535,300 children died of measles in 2000. By 2010, the global push to improve vaccine coverage resulted in a 74% reduction in deaths. These efforts, supported by the Measles & Rubella Initiative (MR Initiative), contributed 23% of the overall decline in under-five deaths between 1990 and 2008 and are driving progress towards meeting MDG4.

The MR Initiative is a collaborative effort of WHO, UNICEF, the American Red Cross, the United States Centers for Disease Control and Prevention, and the United Nations Foundation to control measles and rubella. In April 2012, the MR Initiative launched a new Global Measles and Rubella Strategic Plan which covers the period 2012 - 2020.

2. AVIAN INFLUENZA

Influenza pandemics (outbreaks that affect a large proportion of the world) are unpredictable but recurring events that can have health, economic and social consequences worldwide. An influenza pandemic occurs when key factors converge: an influenza virus emerges with the ability to cause sustained transmission from human-to-human, and there is very low, or no, immunity to the virus among most people. In the interconnected world of today, a localized epidemic can transform into a pandemic rapidly, with little time to prepare a public health response to halt the spread of illness.

Avian influenza (AI) viruses are divided into two groups based on their ability to cause disease in poultry: high pathogenicity or low pathogenicity. Highly pathogenic viruses result in high death rates (up to 100% mortality within 48 hours) in some poultry species. Low pathogenicity viruses also cause outbreaks in poultry but are not generally associated with severe clinical disease.

Key facts

- Avian influenza, commonly called bird flu, is an infectious viral disease of birds.
- Most avian influenza viruses do not infect humans; however some, such as H5N1, have caused serious infections in people.
- Outbreaks of AI in poultry may raise global public health concerns due to their effect on poultry populations, their potential to cause serious disease in people, and their pandemic potential.
- Reports of highly pathogenic AI epidemics in poultry can seriously impact local and global economies and international trade.
- The majority of human cases of H5N1 infection have been associated with direct or indirect contact with infected live or dead poultry. There is no evidence that the disease can be spread to people through properly cooked food.
- Controlling the disease in animals is the first step in decreasing risks to humans.
- Avian influenza (AI) is an infectious viral disease of birds (especially wild water fowl such as ducks and geese), often causing no apparent signs of illness. AI viruses can sometimes spread to domestic poultry and cause large-scale outbreaks of serious disease. Some of these AI viruses have also been reported to cross the species barrier and cause disease or subclinical infections in humans and other mammals.

Avian influenza H5N1 background

The H5N1 virus subtype - a highly pathogenic AI virus- first infected humans in 1997 during a poultry outbreak in Hong Kong SAR, China. Since its widespread re-emergence in 2003 and 2004, this avian virus has spread from Asia to Europe and Africa and has become entrenched in poultry in some countries, resulting in millions of poultry infections, several hundred human cases, and many human deaths. Outbreaks in poultry have seriously impacted livelihoods, the economy and international trade in affected countries. Ongoing circulation of H5N1 viruses in poultry, especially when endemic, continues to pose threats to public health, as these viruses have both the potential to cause serious disease in people and may have the potential to change into a form that is more transmissible among humans. Other influenza virus subtypes also circulate in poultry and other animals, and may also pose potential threats to public health.

Avian influenza H5N1 infections and clinical features in humans

The case fatality rate for H5N1 virus infections in people is much higher compared to that of seasonal influenza infections.

Clinical features

In many patients, the disease caused by the H5N1 virus follows an unusually aggressive clinical course, with rapid deterioration and high fatality. Like most emerging disease, H5N1 influenza in humans is poorly understood.

The incubation period for H5N1 avian influenza may be longer than that for normal seasonal influenza, which is around two to three days. Current data for H5N1 infection indicate an incubation period ranging from two to eight days and possibly as long as 17 days. WHO currently recommends that an incubation period of seven days be used for field investigations and the monitoring of patient contacts.

Initial symptoms include a high fever, usually with a temperature higher than 38 ºC, and other influenza-like symptoms. Diarrhea, vomiting, abdominal pain, chest pain, and bleeding from the nose and gums have also been reported as early symptoms in some patients.

One feature seen in many patients is the development of lower respiratory tract infection early in the illness. On present evidence, difficulty in breathing develops around five days following the first symptoms. Respiratory distress, a hoarse voice, and a crackling sound when inhaling are commonly seen. Sputum production is variable and at times, bloody.

Antiviral treatment

Evidence suggests that some antiviral drugs, notably oseltamivir, can reduce the duration of viral replication and improve prospects of survival.

In suspected cases, oseltamivir should be prescribed as soon as possible (ideally, within 48 hours following symptom onset) to maximize its therapeutic benefits. However, given the significant mortality currently associated with H5N1 infection and evidence of prolonged viral replication in this disease, administration of the drug should also be considered in patients presenting later in the course of illness.

In cases of severe infection with the H5N1 virus, clinicians may need to consider increasing the recommended daily dose or/and the duration of treatment. In severely ill H5N1 patients or in H5N1 patients with severe gastrointestinal symptoms, drug absorption may be impaired. This possibility should be considered when managing such patients.

Risk factors for human infection

The primary risk factor for human infection appears to be direct or indirect exposure to infected live or dead poultry or contaminated environments. Controlling circulation of the H5N1 virus in poultry is essential to reducing the risk of human infection. Given the persistence of the H5N1 virus in some poultry populations, control will require long-term

commitments from countries and strong coordination between animal and public health authorities.

There is no evidence to suggest that the H5N1 virus can be transmitted to humans through properly prepared poultry or eggs. A few human cases have been linked to consumption of dishes made of raw, contaminated poultry blood. However, slaughter, defeathering, handling carcasses of infected poultry, and preparing poultry for consumption, especially in household settings, are likely to be risk factors.

Human pandemic potential

The H5N1 AI virus remains one of the influenza viruses with pandemic potential, because it continues to circulate widely in some poultry populations, most humans likely have no immunity to it, and it can cause severe disease and death in humans. In addition to H5N1, other animal influenza virus subtypes reported to have infected people include avian H7 and H9, and swine H1 and H3 viruses. H2 viruses may also pose a pandemic threat. Therefore, pandemic planning should consider risks of emergence of a variety of influenza subtypes from a variety of sources.

Control and Prevention

Animal health agencies and national veterinary authorities are responsible for the control and prevention of animal diseases, including influenza. WHO, World Organisation for Animal Health (OIE), and Food and Agriculture Organization (FAO) collaborate through a variety of mechanisms to track and assess the risk from animal influenza viruses of public health concern, and to address these risks at the human animal interface wherever in the world they might occur.

3. ENTEROHAEMORRHAGIC ESCHERICHIA COLI (EHEC)

Overview

Escherichia coli (E. coli) is a bacterium that is commonly found in the gut of humans and warm-blooded animals. Most strains of E. coli are harmless. Some strains however, such as enterohaemorrhagic E. coli (EHEC), can cause severe foodborne disease. It is transmitted to humans primarily through consumption of contaminated foods, such as raw or undercooked ground meat products, raw milk and contaminated raw vegetables and sprouts. Its significance as a public health problem was recognized in 1982, following an outbreak in the United States of America.

EHEC produces toxins, known as verotoxins or Shiga-like toxins because of their similarity to the toxins produced by Shigella dysenteriae. EHEC can grow in temperatures ranging from 7°C to 50°C, with an optimum temperature of 37°C. Some EHEC can grow in acidic foods, down to a pH of 4.4, and in foods with a minimum water activity (Aw) of 0.95. It is destroyed by thorough cooking of foods until all parts reach a temperature of 70°C or higher. E. coli O157:H7 is the most important EHEC serotype in relation to public health; however, other serotypes have frequently been involved in sporadic cases and outbreaks.

Key facts

- Enterohaemorrhagic E. coli (EHEC) is a bacterium that can cause severe foodborne disease.
- Primary sources of EHEC outbreaks are raw or undercooked ground meat products, raw milk and faecal contamination of vegetables.
- In most cases, the illness is self-limiting, but it may lead to a life-threatening disease including haemolytic uraemic syndrome (HUS), especially in young children and the elderly.
- EHEC is heat-sensitive. In preparing food at home, be sure to follow basic food hygiene practices such as "cook thoroughly".
- Following the WHO Five keys to safer food is a key measure to prevent infections with foodborne pathogens such as EHEC.

Symptoms

Symptoms of the diseases caused by EHEC include abdominal cramps and diarrhea that may in some cases progress to bloody diarrhea (haemorrhagic colitis). Fever and vomiting may also occur. The incubation period can range from three to eight days, with a median of three to four days. Most patients recover within 10 days, but in a small proportion of patients (particularly young children and the elderly), the infection may lead to a life-threatening disease, such as haemolytic uraemic syndrome (HUS). HUS is characterized by acute renal failure, haemolytic anaemia and thrombocytopenia. It is estimated that up to 10% of patients with EHEC infection may develop HUS, with a case-fatality rate ranging from 3 to 5%. Overall, HUS is the most common cause of acute renal failure in young children. It can cause neurological complications (such as seizure, stroke and coma) in 25% of HUS patients and chronic renal sequelae, usually mild, in around 50% of survivors.

Persons who experience bloody diarrhea or severe abdominal cramps should seek medical care. Antibiotics are not part of the treatment of patients with EHEC disease and may possibly increase the risk of subsequent HUS.

Sources and transmission

Most available information on EHEC relates to serotype O157:H7, since it is easily differentiated biochemically from other E. coli strains. The reservoir of this pathogen appears to be mainly cattle. In

addition, other ruminants such as sheep, goats, deer are considered significant reservoirs, while other mammals (pigs, horses, rabbits, dogs, cats) and birds (chickens, turkeys) have been occasionally found infected.

E. coli O157:H7 is transmitted to humans primarily through consumption of contaminated foods, such as raw or undercooked ground meat products and raw milk. Fecal contamination of water and other foods, as well as cross-contamination during food preparation (with beef and other meat products, contaminated surfaces and kitchen utensils), will also lead to infection. Examples of foods implicated in outbreaks of E. coli O157:H7 include undercooked hamburgers, dried cured salami, unpasteurized fresh-pressed apple cider, yogurt, cheese made from raw milk.

An increasing number of outbreaks are associated with the consumption of fruits and vegetables (sprouts, spinach, lettuce, coleslaw, salad) whereby contamination may be due to contact with faeces from domestic or wild animals at some stage during cultivation or handling. EHEC has also been isolated from bodies of water (ponds, streams), wells and water troughs, and has been found to survive for months in manure and water-trough sediments. Waterborne transmission has been reported, both from contaminated drinking-water and from recreational waters.

Person-to-person contact is an important mode of transmission through the oral-faecal route. An asymptomatic carrier state has been reported, where individuals show no clinical signs of disease but are capable of infecting others. The duration of excretion of EHEC is about one week or less in adults, but can be longer in children. Visiting farms and other venues where the general public might come into direct contact with farm animals has also been identified as an important risk factor for EHEC infection.

Prevention

The prevention of infection requires control measures at all stages of the food chain, from agricultural production on the farm to processing, manufacturing and preparation of foods in both commercial establishments and household kitchens.

Industry

The number of cases of disease might be reduced by various mitigation strategies for ground beef (for example, screening the animals pre-slaughter to reduce the introduction of large numbers of pathogens in the slaughtering environment). Good hygienic slaughtering practices reduce contamination of carcasses by faeces, but do not guarantee the absence of EHEC from products. Education in hygienic handling of foods for workers at farms, abattoirs and those involved in the food production is indispensable to keep microbiological contamination to a minimum level.

The only effective method of eliminating EHEC from foods is to introduce a bactericidal treatment, such as heating *(e.g.* cooking, pasteurization) or irradiation.

Household

Preventive measures for E. coli O157:H7 infection are similar to those recommended for other foodborne diseases. Basic good food hygiene practice, as described in the WHO Five keys to safer food, can prevent the transmission of pathogens responsible for many foodborne diseases, and also protect against foodborne diseases caused by EHEC. Such recommendations should in all cases be implemented, especially "Cook thoroughly" so that the centre of the food reaches at least 70 °C. Make sure to wash fruits and vegetables carefully, especially if they are eaten raw. If possible, vegetables and fruits should be peeled. Vulnerable populations (e.g. small children, the elderly) should avoid the consumption of raw or undercooked meat products, raw milk and products made from raw milk.

Regular hand washing, particularly before food preparation or consumption and after toilet contact, is highly recommended, especially for people who take care of small children, the elderly or immunocompromised individuals, as the bacterium can be passed from person-to-person, as well as through food, water and direct contact with animals.

Since a number of EHEC infections have been caused by contact with recreational water, it is very important to protect such water areas, as well as drinking-water sources, from animal waste.

WHO response

During E. coli outbreaks, such as the ones in Europe in 2011, WHO has responded by:

- supporting the coordination of information sharing and collaboration through International Health Regulations and the International Food Safety Authorities Network (INFOSAN) worldwide;
- working closely with national health authorities and international partners, providing technical assistance and the latest information on the outbreak.
- In terms of prevention, WHO has responded with a global strategy to decrease the burden of foodborne diseases. WHO developed the Five keys to safer food message. The Five keys and associated training materials provide countries with materials that are easy to use, reproduce and adapt to different target audiences.

4. DEMENTIA CASES SET TO TRIPLE BY 2050 BUT STILL LARGELY IGNORED

About dementia and Alzheimer's disease

Dementia is a syndrome that can be caused by a number of progressive disorders caused by a variety of brain illnesses that affect memory, thinking, behaviour and the ability to perform everyday activities. Alzheimer's disease is the most common cause of dementia.

The number of people living with dementia worldwide is currently estimated at 35.6 million. This number will double by 2030 and more than triple by 2050. Dementia is overwhelming not only for the people who have it, but also for their caregivers and families. There is a lack of awareness and understanding of dementia in most countries, resulting in stigmatization, barriers to diagnosis and care, and impacting caregivers, families and societies physically, psychologically and economically.

10 Facts on Dementia

Dementia is not a normal part of ageing: Although dementia mainly affects older people, it is not a normal part of ageing. Dementia is a syndrome, usually of a chronic or progressive nature, caused by a variety of brain illnesses that affect memory, thinking, behaviour and ability to perform everyday activities.

35.6 million people live with dementia: The total number of people with dementia worldwide in 2010 is estimated at 35.6 million. Among them, 58% live in low- and middle-income countries, and this proportion is projected to rise to 71% by 2050.

A new case of dementia is diagnosed every 4 seconds: The total number of new cases of dementia each year worldwide is nearly 7.7 million, implying one new case every four seconds. The number of people with dementia is expected to nearly double every 20 years, to 65.7 million in 2030 and 115.4 million in 2050.

Huge economic impact; US$ 604 billion per year: The high cost of the disease will challenge health systems to deal with the predicted future increase of cases. The costs are estimated at US$ 604 billion per year at present and are set to increase even more quickly than the prevalence.

Caregivers of dementia patients experience high strain: Caring for dementia patients is overwhelming for caregivers. The stresses include physical, emotional and economic pressures. Care givers require support from the health, social, financial and legal systems.

Early diagnosis improves the quality of life of people with dementia and their families:

The principal goals for dementia care are:

- diagnosing cases early;
- optimising physical health, cognition, activity and well-being;
- detecting and treating behavioural and psychological symptoms; and
- providing information and long-term support to caregivers.

People with dementia and their families are often discriminated against: People with dementia are frequently denied the basic rights and freedoms available to others. For example, physical and chemical restraints are used extensively in aged-care facilities and acute-care settings.

Awareness and advocacy are needed: Improving the awareness and understanding of dementia across all levels of society is needed to decrease discrimination and to improve the quality of life for people with dementia and their caregivers.

More research and evaluation is required: More research is needed to develop new and more effective treatments and to better understand the causes of dementia. Research that identifies the modifiable risk factors of dementia is still scarce.

Dementia is a public health priority: To address this important health priority there are actions that can be taken:

- promote a dementia friendly society;
- make dementia a public health and social care priority everwhere;
- improve attitudes to, and understanding of, dementia;
- invest in health and social systems to improve care and services for people with dementia and their caregivers; and
- increase research on dementia.

Treating and caring for people with dementia currently costs the world more than US$ 604 billion per year. This includes the cost of providing health and social care as well the reduction or loss of income of people with dementia and their caregivers.

Only eight countries worldwide currently have national programs in place to address dementia. A new report "Dementia: a public health priority", published by the World Health Organization (WHO) and Alzheimer's Disease International, recommends that programs focus on improving early diagnosis; raising public awareness about the disease and reducing stigma; and providing better care and more support to caregivers.

Lack of diagnosis is a major problem. Even in high-income countries, only one- fifth to one- half of cases of dementia are routinely recognized. When a diagnosis is made, it often comes at a relatively late stage of the disease.

"We need to increase our capacity to detect dementia early and to provide the necessary health and social care. Much can be done to decrease the burden of dementia," says Dr Oleg Chestnov, Assistant Director-General, Noncommunicable Diseases and Mental

Health at WHO. "Health-care workers are often not adequately trained to recognize dementia."

The report points to a general lack of information and understanding about dementia. This fuels stigma, which in turn contributes to the social isolation of both the person with dementia and their caregivers, and can lead to delays in seeking diagnosis, health assistance and social support.

"Public awareness about dementia, its symptoms, the importance of getting a diagnosis, and the help available for those with the condition is very limited. It is now vital to tackle the poor levels of public awareness and understanding, and to drastically reduce the stigma associated with dementia," says Marc Wortmann, Executive Director, Alzheimer's Disease International.

Strengthening care is also a key. In every region of the world, most care-giving is provided by informal caregivers - spouses, adult children, other family members and friends. The report notes that people who care for a person with dementia are themselves particularly prone to mental disorders, such as depression and anxiety, and are often in poor physical health themselves. Many caregivers also suffer economically as they may be forced to stop working, cut back on work, or take a less demanding job to care for a family member with dementia.

The report recommends involving existing caregivers in designing programs to provide better support for people with dementia and those looking after them. Community-based services can provide valuable support to families caring for people with dementia in both high- and low-income countries - delaying the need for people to enter into high-cost residential care. At the same time, health workforce training needs to pay closer attention to dementia, and the skills required to provide both clinical and long-term care.

Dementia is a syndrome, usually of a chronic nature, caused by a variety of brain illnesses that affect memory, thinking, behaviour and ability to perform everyday activities. Alzheimer's disease is the most common cause of dementia and possibly contributes to up to 70% of cases. Although dementia affects people in all countries, more than half (58%) live in low- and middle-income countries. This is likely to rise to more than 70% by 2050.

For more information contact: Fadéla Chaib, WHO Communications officer. Telephone: + 41 22 791 32 28; Mobile: + 41 79 475 55 56; Email: chaibf@who.int

Dementia: http://www.who.int/mental_health/publications/dementia_report_2012
www.alz.co.uk/about-dementia.

5. CARDIOVASCULAR DISEASES (CVDS)

What are cardiovascular diseases?

Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels and include:

- coronary heart disease – disease of the blood vessels supplying the heart muscle
- cerebrovascular disease - disease of the blood vessels supplying the brain
- peripheral arterial disease – disease of blood vessels supplying the arms and legs
- rheumatic heart disease – damage to the heart muscle and heart valves from rheumatic fever, caused by streptococcal bacteria
- congenital heart disease - malformations of heart structure existing at birth
- deep vein thrombosis and pulmonary embolism – blood clots in the leg veins, which can dislodge and move to the heart and lungs.

Heart attacks and strokes are usually acute events and are mainly caused by a blockage that prevents blood from flowing to the heart or brain. The most common reason for this is a build-up of fatty deposits on the inner walls of the blood vessels that supply the heart or brain. Strokes can also be caused by bleeding from a blood vessel in the brain or from blood clots.

Key Facts

- CVDs are the number one cause of death globally: more people die annually from CVDs than from any other cause.
- An estimated 17.3 million people died from CVDs in 2008, representing 30% of all global deaths. Of these deaths, an estimated 7.3 million were due to coronary heart disease and 6.2 million were due to stroke.
- Low- and middle-income countries are disproportionally affected: over 80% of CVD deaths take place in low- and middle-income countries and occur almost equally in men and women.
- By 2030, almost 23.6 million people will die from CVDs, mainly from heart disease and stroke. These are projected to remain the single leading causes of death.

What are the risk factors for cardiovascular disease?

The most important behavioural risk factors of heart disease and stroke are unhealthy diet, physical inactivity, tobacco use and harmful use of alcohol. Behavioural risk factors are responsible for about 80% of coronary heart disease and cerebrovascular disease.

The effects of unhealthy diet and physical inactivity may show up in individuals as raised blood pressure, raised blood glucose, raised blood lipids, and overweight and obesity; these are called 'intermediate

risk factors' or metabolic risk factors. There are also a number of underlying determinants of CVDs, or "the causes of the causes".

What are common symptoms of cardiovascular diseases?

Symptoms of heart attacks and strokes: Often, there are no symptoms of the underlying disease of the blood vessels. A heart attack or stroke may be the first warning of underlying disease. Symptoms of a heart attack include:

- pain or discomfort in the centre of the chest;
- pain or discomfort in the arms, the left shoulder, elbows, jaw, or back.

The most common symptom of a stroke is sudden weakness of the face, arm, or leg, most often on one side of the body. Other symptoms include sudden onset of: numbness of the face, arm, or leg, especially on one side of the body; confusion, difficulty speaking or understanding speech; difficulty seeing with one or both eyes; difficulty walking, dizziness, loss of balance or coordination; severe headache with no known cause; and fainting or unconsciousness. People experiencing these symptoms should seek medical care immediately.

What is rheumatic heart disease?

Rheumatic heart disease is caused by damage to the heart valves and heart muscle from the inflammation and scarring caused by rheumatic fever. Rheumatic fever is caused by streptococcal bacteria, which usually begins as a sore throat or tonsillitis in children.

Symptoms of rheumatic heart disease

- Shortness of breath, fatigue, irregular heart beats, chest pain and fainting.
- Symptoms of rheumatic fever: fever, pain and swelling of the joints, nausea, stomach cramps and vomiting.

Treatment

Early treatment of streptococcal sore throat can stop the development of rheumatic fever. Regular long-term penicillin treatment can prevent repeat attacks of rheumatic fever which give rise to rheumatic heart disease and can stop disease progression in people whose heart valves are already damaged by the disease.

Why are cardiovascular diseases a development issue in low- and middle-income countries?

- Over 80% of the world's deaths from CVDs occur in low- and middle-income countries.
- People in low- and middle-income countries are more exposed to risk factors leading to CVDs and other noncommunicable diseases and are less exposed to prevention efforts
- People in low- and middle-income countries have less access to effective and equitable health care services which respond to their needs (including early detection services).
- As a result, many people in low- and middle-income countries die younger from CVDs and other noncommunicable diseases
- The poorest people in low- and middle-income countries are affected most. At household level, sufficient evidence is emerging to prove that CVDs and other noncommunicable diseases contribute to poverty.
- At macro-economic level, CVDs place a heavy burden on the economies of low- and middle-income countries.

How can the burden of cardiovascular diseases be reduced?

Heart disease and stroke can be prevented through healthy diet, regular physical activity and avoiding tobacco smoke. Individuals can reduce their risk of CVDs by engaging in regular physical activity, avoiding tobacco use and second-hand tobacco smoke, choosing a diet rich in fruit and vegetables and avoiding foods that are high in fat, sugar and salt, and maintaining a healthy body weight.

6. WORLD MALARIA DAY 2012

Test, Treat, Track: scaling up the fight against malaria

On the eve of World Malaria Day 2012, WHO hails global progress in combating malaria but highlights the need to further reinforce the fight. WHO's new initiative, T3: Test, Treat, Track, urges malaria-endemic countries and donors to move towards universal access to diagnostic testing and antimalarial treatment, and to build robust malaria surveillance systems.

A million lives saved

"In the past ten years, increased investment in malaria prevention and control has saved more than a million lives," says Dr Margaret Chan, WHO Director-General. "This is a tremendous achievement. But we are still far from achieving universal access to life-saving malaria interventions."

Progress not enough to meet target

A massive acceleration in the global distribution of mosquito nets, the expansion of programs to spray the insides of buildings with insecticides, and an increase in access to prompt antimalarial treatment has brought down malaria mortality rates by more than a quarter worldwide, and by one third in Africa since 2000. But simply maintaining current rates of

progress will not be enough to meet global targets for malaria control.

T3: Test, Treat, Track

WHO therefore urges the global health community to further scale up investments in diagnostic testing, treatment, and surveillance for malaria in order to save more lives and to make a major push towards achieving the health-related Millennium Development Goals in 2015. Endemic countries should be able to ensure that every suspected malaria case is tested, that every confirmed case is treated with a quality-assured antimalarial medicine, and that the disease is tracked through timely and accurate surveillance systems.

WHO has published technical guidance for all three pillars of T3: Test, Treat, Track – releasing the final two documents of the package, Disease Surveillance for Malaria Control, and Disease Surveillance for Malaria Elimination, today.

"Until countries are able to test, treat, and report every malaria case, we will never defeat this disease," says Dr Margaret Chan, who is in Namibia for World Malaria Day this year. "We need strong and sustained political commitment from all countries where malaria is endemic, and from the global health community, to see this fight through to the end."

- In half of all malaria-endemic countries in Africa, over 80% of cases are still being treated without diagnostic testing. Universal diagnostic testing will ensure that patients with fever receive the most appropriate treatment, and that antimalarial medicines are used rationally and correctly. Countries that have already scaled up diagnostic testing (such as Senegal) are saving hundreds of thousands of treatment courses every year.
- Many countries have made significant progress in improving access to antimalarials. In 2010, 60 governments were providing artemisinin-based combination therapies (ACTs) free of charge to all age groups. But millions of people still lack ready access to appropriate treatment. The effort must be scaled up to ensure that every confirmed malaria case gets treated.
- Improved surveillance for malaria cases and deaths will help countries determine which areas or population groups are most affected. It will also help ministries of health to identify resurgences and map new trends - thus maximizing the efficiency of prevention and control programs. Better surveillance will also allow for a more effective delivery of international aid programs.

"T3: Test, Treat, Track aims to galvanize endemic countries and their partners to build on the success of malaria prevention efforts over the past decade," says Dr Robert Newman, Director of WHO's Global Malaria Programme. "In recent years, there has been major progress in the development of new diagnostic tools and highly effective antimalarial medicines. The challenge now is to ensure these tools get used, and that countries accurately measure their public health impact."

Malaria progress, 2000-2010

During the past decade, global malaria prevention and control efforts have been scaled up, with notable progress in sub-Saharan Africa, where the vast majority of malaria cases occur. The number of long-lasting insecticidal nets delivered to malaria-endemic countries in sub-Saharan Africa increased from 5.6 million in 2004 to 145 million in 2010. Programs to spray the interiors of buildings with insecticides were also expanded, with the number of people protected in sub-Saharan Africa rising from 10 million in 2005 to 81 million in 2010.

The availability of rapid diagnostic tests has made it possible to improve and expand diagnostic testing for malaria. The rate of testing - in the public sector in Africa - rose from less than 5% in 2000 to 45% in 2010. Meanwhile, the number of ACTs procured worldwide by government health departments also increased exponentially: from 11 million in 2005 to 181 million in 2010. However, malaria transmission still occurs in 99 countries around the world, and the malaria burden continues to cripple health systems in many African countries. In 2010, this entirely preventable and treatable disease caused an estimated 655 000 deaths worldwide. About 560 000 of the victims were children under five years of age, which means malaria killed one child every minute.

World Malaria Day was instituted by the World Health Assembly at its 60th session in May 2007 to recognize the global effort to provide effective control of malaria. It is celebrated on 25 April ever year.

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7. ORAL HEALTH

Oral health is essential to general health and quality of life. It is a state of being free from mouth and facial pain, oral and throat cancer, oral infection and sores, periodontal (gum) disease, tooth decay, tooth loss, and other diseases and disorders that limit an individual's capacity in biting, chewing, smiling, speaking, and psychosocial wellbeing.

Key facts

- Worldwide, 60–90% of school children and nearly 100% of adults have dental cavities.

- Dental cavities can be prevented by maintaining a constant low level of fluoride in the oral cavity.
- Severe periodontal (gum) disease, which may result in tooth loss, is found in 15 – 20% of middle-aged (35-44 years) adults.
- Globally, about 30% of people aged 65 – 74 have no natural teeth.
- Oral disease in children and adults is higher among poor and disadvantaged population groups.
- Risk factors for oral diseases include an unhealthy diet, tobacco use, harmful alcohol use and poor oral hygiene, and social determinants.

Oral diseases and conditions

The most common oral diseases are dental cavities, periodontal (gum) disease, oral cancer, oral infectious diseases, trauma from injuries, and hereditary lesions.

Dental cavities

Worldwide, 60 – 90% of school children and nearly 100% of adults have dental cavities, often leading to pain and discomfort.

Periodontal disease

Severe periodontal (gum) disease, which may result in tooth loss, is found in 15 – 20% of middle-aged (35 - 44 years) adults.

Tooth loss

Dental cavities and periodontal disease are major causes of tooth loss. Complete loss of natural teeth is widespread and particularly affects older people. Globally, about 30% of people aged 65 – 74 have no natural teeth.

Oral cancer

The incidence of oral cancer ranges from one to 10 cases per 100 000 people in most countries. The prevalence of oral cancer is relatively higher in men, in older people, and among people of low education and low income. Tobacco and alcohol are major causal factors.

Fungal, bacterial or viral infections in HIV

Almost half (40 – 50%) of people who are HIV-positive have oral fungal, bacterial or viral infections. These often occur early in the course of HIV infection.

Oro-dental trauma

Across the world, 16 - 40% of children in the age range 6 - 12 years old are affected by dental trauma due to unsafe playgrounds, unsafe schools, road accidents, or violence.

Noma

Noma is a gangrenous lesion that affects young children living in extreme poverty primarily in Africa and Asia. Lesions are severe gingival disease followed by necrosis (premature death of cells in living tissue) of lips and chin. Many children affected by noma suffer from other infections such as measles and HIV. Without any treatment, about 90% of these children die.

Cleft lip and palate

Birth defects such as cleft lip and palate occur in about one per 500 – 700 of all births. This rate varies substantially across different ethnic groups and geographical areas.

Common causes

Risk factors for oral diseases include an unhealthy diet, tobacco use and harmful alcohol use. These are also risk factors for the four leading chronic diseases – cardiovascular diseases, cancer, chronic respiratory diseases and diabetes – and oral diseases are often linked to chronic disease. Poor oral hygiene is also a risk factor for oral disease.

The prevalence of oral disease varies by geographical region, and availability and accessibility of oral health services. Social determinants in oral health are also very strong. The prevalence of oral diseases is increasing in low- and middle-income countries, and in all countries, the oral disease burden is significantly higher among poor and disadvantaged population groups.

Prevention and treatment

The burden of oral diseases and other chronic diseases can be decreased simultaneously by addressing common risk factors. These include:

- decreasing sugar intake and maintaining a well-balanced nutritional intake to prevent tooth decay and premature tooth loss;
- consuming fruit and vegetables that can protect against oral cancer;
- stopping tobacco use and decreasing alcohol consumption to reduce the risk of oral cancers, periodontal disease and tooth loss;
- ensuring proper oral hygiene;
- using protective sports and motor vehicle equipment to reduce the risk of facial injuries; and
- safe physical environments.

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