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- Blunt Cerebrovascular Injuries - A review of literature
- Umbilical Cord Blood Banking and Transplantation - A short review
- Neonatal Screening - Mean haemoglobin and red cell indices in cord blood from Omani neonates
- Simultaneous Detection of Dengue NS1 Antigen, IgM plus IgG and Platelet Enumeration during an Outbreak
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Please note that from January 2012 SQUMJ will be moving to the **Editorial Manager** online manuscript submission and review system. Our website will have instructions on how to use this system.
In this issue of the journal, Dr. Saleh Al-Hinai and colleagues have published their results on a survey studying the medical tourism patterns of patients going abroad from the Al-Dakhilya Region of Oman. They managed to obtain 40 responses to the 45 questionnaires they distributed. Basically, most of the results they obtained from the patients in their region who had sought treatment abroad were similar to those of other studies: 10% of the respondents went for treatment plus tourism, and 2.5% were healthy. Strikingly, 15% of the patients experienced complications after their treatment abroad and this is not an unusual finding in the literature. Only a few of the patient’s in Al-Hinai’s study used the Internet and the available medical tourism offices to obtain information on treatment abroad options instead the majority relied on word of mouth advice from friends. Most of the patients went to Thailand, and orthopaedic conditions were the most common indication for these patients to seek treatment abroad. This article is of special interest to Oman and should stimulate discussion on the advantages and disadvantages of going abroad for medical services. What are its advantages and disadvantages to the patients, and to Omani health services? Likewise, what are the advantages and the disadvantages to the host country?

Medical tourism is part of health tourism and it has a long-standing history, going back to thousands of years. Records show that in Greece, thousands of years ago, patients came to the healing god Asklepios in Epidauria. At the same time in other countries, people used to travel to therapeutic spas and collect waters from holy shrines. Much more recently, in the 18th century, health spas were a common feature of medical tourism. Health tourism, which includes medical tourism, is generally defined as organised travel outside one’s local environment for the maintenance, enhancement, or restoration of an individual’s well-being in mind and body. Medical tourism is regarded as more organised travel outside one’s natural health care jurisdiction. Typically it is linked with engagement in leisure, businesses and other purposes.

There are several types of medical tourism, and they are classified in many ways. One such classification includes: 1) “Temporary visitors abroad” who go for either check-up or treatment; 2) “Long-term residents” e.g. people who move to a location better for their health like many Americans who go to Florida or the Caribbean; 3) “Medical tourist, from 2 adjacent countries who share common borders” and have agreed upon sharing health care, and 4) “Outsourced patients” — these are patients who are sent abroad by their government, as the neither necessary treatment nor the specialist is available locally. This last definition fits many Omani patients.

Why do patients go abroad? Jagyasi gave 5 major “factors” involved in decision making: affordable, accessible, available, acceptable and additional. Affordable is probably the major reason and this is particularly true for patients from the well-off, developed countries like America and UK, where private health care is expensive, and some surgeries...
are not covered by their insurance. *Available* is often because the medical treatment they need is not available in their local areas or not trusted by the patients, as is often the case with Omani patients. *Accessible* applies more particularly to patients from countries where the waiting list is long, particularly to national health service patients in the UK and in Canada. In the UK, private health care may be available locally, but is expensive. *Acceptable* applies to services, which may be affordable, available, and accessible, but they are not acceptable in the patient’s own country for religious, political reasons or other social reasons. *Additional* refers to the availability of better care, perhaps better technology, or a better specialist, or simply better service and personalised care abroad compared to care in the home country.

There are several reasons, related to above, why patients choose to become medical tourists. For the Americans and Europeans the attraction is value, i.e. affordability. For example the price of a coronary artery bypass graft (CABG) is $113,000 in the USA, but only $10,000 in India; heart valve replacements cost $150,000 in USA, but $9,500 in India, and knee replacements cost $48,000 in the States, but only $8,500 in India. Most references quote the prices of surgery in India, Thailand and Singapore as only 5% to 10% of the prices in the USA. A forecast by Deloitte Consulting published in August 2008 projected that medical tourism originating in the US could jump by a factor of 10 over the next decade.

However, besides the financial benefit, there are other advantages for a patient to have treatment abroad in a centre of excellence for certain conditions. Many of the countries seeking to develop medical tourism invite specialists from well-known health care centres such as Columbia and Cleveland Clinic, Mayo Clinic, Harvard Medical International, and are thus able to offer excellent medical care. Many of them are encouraged and supported by their host governments, e.g. India has introduced a special M-Visa category for medical tourists. Malaysia’s Ministry of Health has formed a special national committee for the promotion of health tourism. This has contributed to the reversal of the geographical trend of medical tourism. In the past, patients from the east were travelling to the west to get the best medical treatment. Now, patients from Western developed countries, travel east to developing countries for the best medical and technologically advanced health care. Eastern Europe has now joined the bandwagon including Hungary and Poland which are popular for dental work.

However, there are several problems with medical tourism as discussed by several agencies and scholars. These include poor or no follow-up care. After being in hospital for a short while and having a vacation, the patient comes home with, perhaps, complications of the surgery or side effects of the drugs. It is a surgical principle that every surgeon looks after his own complications and obviously that does not apply for most if not all patients who have been treated abroad. Many countries have very weak malpractice laws and thus patients have limited ability to complain about poor medical care. Medical tourism also affects the host countries with the problem of internal brain drain, whereby all good doctors give up serving the public sector to go into the exotic, private health centres, which serve the medical tourists. Thailand’s Bumrungrad Hospital, which treats about more than half a million international patients a year, is a major source of internal brain drain, leading to a political discussion within Thailand and a National Public Radio (NPR, USA) special programme on the shortage of Thai doctors in Bangkok because of the higher pay offered by Bumrungrad. Thus, globalisation impacts world health care, both in the host and the donor countries.

There are other risks which medical tourism poses to patients. For example, patients may not tolerate travel very well, or may not have inherent resistance to some of the diseases in the host countries. We therefore need to have better scientific studies on the impact of medical tourism on the health care services of the source and destination countries as well as on the patients themselves. We need more statistics on the rate of complications. The article in this issue of this journal reported a 15% complication rate; granted we do not know how severe those complications were, but that is what needs to be studied. A survey was carried out by the British Association of Plastic, Reconstructive and Aesthetic Surgery. They received responses from 203 out of 325 members. A total of 37% of them had seen a patient in the National Health Service with complications arising from overseas cosmetic surgery. In another survey in the UK, 60% of complications were of emergency
nature requiring inpatient admission. Americans and Europeans now realise that they need to analyse the impact of medical tourism—beneficent or maleficent—on the patients and the country’s health care system.

Many medical tourists are satisfied, but satisfaction does not always parallel good outcome. Often satisfaction can simply be a result of good service. It is of special interest to note that “outsourced patients,” those who were sent by the government are often dissatisfied with the total experience compared to the true self-financed medical tourist. That is why an institution has to be accredited for good medical care with a good quality assurance programme rather than just good service. Now more and more of the provider institutions try for accreditation by either the Joint Commission International (JCI) or Trent or for Canadian accreditation. The JCI has accredited Wockhardt Hospital in India and several other institutions.

Patients going abroad need to get good advice. According to the World Tourism Organization’s Global Code of Ethics for Tourism, tourists should have the same rights as citizens of destination countries. Unfortunately, that is not always the case and that is another potential source of problems. For example, personal data is stored electronically and may not be treated as confidentially as the patients have a right to expect. We have no control over that when patients go abroad. Another major problem is informed consent. Is it always informed?

A further potential significant problem with medical tourism is that sometimes it impacts the source country’s health care system. A source country may become complacent by being able to send its citizens abroad for certain procedures and thus fail to develop the appropriate national services. The development of positron emission tomography (PET) in Oman is an example of this. This has been delayed for years now as patients are simply sent abroad for PET imaging. Sending patients abroad is not only costly to the government, but it also dilutes the political support and the will to develop certain essential national services. This situation often helps create a 2-tier system in the destination country whereby the local population receives second-class treatment while medical tourist gets much better treatment in the more sophisticated, well-equipped, state-of-the-art hospitals.

Among the disadvantages of medical tourism is the one related to health insurance companies, who may refuse to cover a patient going abroad for legitimate reasons, or may actually encourage patients to go abroad if the treatment is cheaper, but then not cover the airfare and other expenses. The other side of the coin is that there is now pressure on insurance companies to cover the cost of all overseas treatment and this may mean raising premiums—yet another negative side to medical tourism for some patients.

The organisations that provide accreditation need to consult with each other and establish a uniform, or at least a fairly similar level of accreditation to ensure that the patient is the winner. They can do that only if they share experiences, ideas and methodology. One of the problems of medical tourism is that it generally raises the cost of health care in the host country. For example, India claims that they are improving the services for the local citizens by having more tourists and improving the health care in those tourist centres. But, the truth is that in most places, and certainly in almost all small towns and villages in India, they do not have even labour rooms and people suffer from severely overcrowded hospitals where patient bed space is both under as well as on the bed. This is exacerbated by the internal brain drain of hospital administrators and of doctors described above.

One of the major concerns related to medical tourism is the ethical aspects of treatment. These should be examined and the risks discussed with the patient, but, on the other hand, it is important that patients have their own autonomy in decision-making. Beneficence and nonmaleficence are the basis of medical ethics. Thus it is our responsibility to promote patients’ welfare, treat them with justice and improve their health while we avoiding harming them. These ethical principles are not easily upheld in the delicate balance of commerce versus medical ethics. Another aspect of medical ethics is the ownership of responsibility for treating the complications of the treatment given abroad. Another ethical consideration is that each country may have a different standard of medical ethics. For example, what is considered experimental therapy in one country, like stem cell therapy, is routinely used in the private institutions providing care for medical tourists in other countries. Likewise, the medical ethics related to organ transplantation differ from country to country. While most
countries do not allow the involvement of money in organ donation, it is a common practice in some countries, and donors can even be a living non-relative. The Declaration of Istanbul on Organ Trafficking and Transplantation Tourism, 2008, has condemned organ transplant tourism.12

It is the responsibility of the medical profession to stop the trend of treating medicine and health care like goods and services traded in business.13,14 Burney has pointed out in SQUMJ that medical tourism may receive "uncalled for treatment".15 The quality assurance trend in health care has introduced the term "consumer" to describe patients in an effort to improve the quality of care in hospitals. Unfortunately, the term "health consumer" is now misused in the business of delivery of health care.

The quality and safety of medical treatment abroad has to be studied and questioned and it should be under the scrutiny of the medical profession and the Ministry of Health in Oman. Unless we have good grip on the quality of the care that our patients are receiving abroad, their safety may be at risk. We need more statistics, better studies and better reporting systems. The question of who will look after these patients when they return, has not been answered, but must be tackled.

Thus, there is a major lack of systematic data about health services provided abroad, not only for Omanis, but, also for citizens of many other countries. More organised studies are needed and specifically outcome studies. Research into the delivery of health care has not yet adequately evaluated medical tourism. The issue of lack of data must be taken very seriously. Medical tourism has some benefits, but there are more problems with it and, as physicians, we have to keep in mind our basic principles of beneficence and nonmaleficence.

References
Trauma caused by motor vehicle collisions (MVCs) is currently the third most common cause of death globally, with 90% of these deaths occurring in developing countries including Oman. In fact, Oman has one of the highest rates of deaths from MVCs in the world, with a mortality rate of 20–30 per 100,000.1

Some injuries may be evident at the time of admission, while another class of injuries may remain occult for some time and then become evident when it may be too late for any intervention.

Blunt cerebrovascular injuries (BCVIs) are one of the occult injuries caused by blunt trauma. They are considered to be relatively uncommon; however, they carry a high rate of mortality and morbidity if they remain undetected.

BCVIs may or may not initially present with symptoms or signs that warrant suspicion of such injuries and therefore the provision of adequate diagnostic investigations and management is crucial. The realisation of this fact led to increased awareness of the amplitude of such injuries and the need to establish adequate screening criteria and cost-effective screening modalities.

If symptoms do present, however, they are usually attributable to focal neurological deficits.
caused by ischaemia of the carotid or vertebral artery territories, or are due to a traumatic carotid-cavernous fistula manifesting as orbital pain, proptosis, hyperaemia, cerebral swelling, or seizure.2

Incidence of BCVIs
The general incidence of BCVIs amongst all trauma admissions has been reported in the literature as <1%. The incidence of blunt carotid artery injuries (BCIs) reported in the literature ranges from 0.08–0.27% while the incidence of blunt vertebral artery injuries (BVIs) ranges from 0.20% to 0.77%.3,4 Although these patients are a small fraction of all trauma patients, they carry risks of stroke and mortality that are as high as 58% and 59% respectively.5,6,7

Mechanism of Injury
The three basic mechanisms of injury to the cerebrovascular vessels are: 1) Severe hyperextension and rotation; 2) Direct blow to the vessel, and 3) Vessel laceration by adjacent bone fractures.2 Injuries to the extracranial carotid artery are most commonly due to hyperextension of the vessel over the lateral articular processes of C 1–3 at the base of the skull. Direct blows to the vessels in seat-belt injuries and hanging attempts are also possible causes. Injuries to the intracranial segment of the carotid artery are mostly due to basal skull fractures.2 Vertebral artery injuries occur most commonly in fractures involving the course of the vessel through the transverse foramina of C 2–6.2

Pathogenesis
With any of the mechanisms of injury mentioned above, the pathological changes in the vessels are that of intimal disruption, dissection, pseudoaneurysm formation, carotid-cavernous fistula, thrombosis and complete transection of the artery.2,3 The resultant ischaemia caused by these injuries is thought to be due to the following: 1) Dissection of the artery causing haemodynamic instability, and 2) Intimal disruption exposing subendothelial collagen fibres and promoting platelet aggregation, subsequent thrombosis and thromboembolism.3

Is Screening Necessary?
Given the possible catastrophic implications of these injuries, the very high stroke rate in this population, and the increased awareness amongst health care professionals, the following question has been raised among investigators: "Is it necessary to implement screening protocols for patients at high risk of these injuries?"

The argument proposed by some investigators, who disagree with the implementation of screening protocols, is that screening this population of patients is not very cost-effective, nor does it really affect the outcome. In addition, after exposing the patient to aggressive screening and the risks of invasive digital subtraction angiography, a decision on treatment with anticoagulation therapy, interventional angiography or surgery is not always feasible. This would be because of the other morbidities from which patients of blunt trauma usually suffer, such as head injuries.9

However, other investigators attempted to prove that aggressive screening and early intervention is indeed justified and cost-effective. In a prospective analysis, between January 1996 and June 2004, Cothren et al., screened 727 patients with blunt trauma who had injuries highly suspicious of an underlying BCVI, (according to comprehensive screening criteria) and underwent a 4-vessel cerebrovascular angiogram. Of these patients, 244 were identified as having BCVIs. Antithrombotic therapy was immediately started in the 187 asymptomatic patients who had no contraindications. Using the estimated stroke risk stratification according to the degree of carotid artery injury found on angiography [Table 1],10

Table 1: Blunt cerebrovascular injuries grading scale

<table>
<thead>
<tr>
<th>Injury grade</th>
<th>Angiographic findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Luminal irregularity or a dissection/intramural haematoma with &lt;25% luminal narrowing</td>
</tr>
<tr>
<td>II</td>
<td>Dissection or intramural haematoma of 25% of the lumen</td>
</tr>
<tr>
<td>III</td>
<td>Pseudoaneurysm</td>
</tr>
<tr>
<td>IV</td>
<td>Vessel occlusion</td>
</tr>
<tr>
<td>V</td>
<td>Vessel transection</td>
</tr>
</tbody>
</table>

Source: Cothren, et al.10
Blunt Cerebrovascular Injuries
A review of literature

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BCVIs among all blunt trauma patients identified in their institution.6 Using the Memphis criteria, 3.5% of patients were screened with BCVIs identified in 29% of them. The overall incidence of BCVIs in this study was found to be 1.03%.11

Modalities of Screening

Screening criteria are based on recognising types of injury mechanisms that have been shown to be highly associated with BCVIs. The advent of multi-slice computed tomography (CT) scanners has enabled eligible patients to undergo screening with a sensitivity and specificity that is comparable to angiography, the gold standard screening tool. The treatment of most injuries is anticoagulation and in some instances, wherever indicated, endovascular therapy might be the best choice.

D I G I T A L  S U B T R A C T I O N  A N G I O G R A P H Y  ( D S A )

Digital subtraction angiography (DSA) is considered to be the gold-standard diagnostic modality to detect BCVIs12,13 yet it carries a risk of serious complications given that it is an invasive modality. The risks attributable to DSA are similar to those of stroke and haemorrhage. The latter limitations and the fact that DSA is expensive and technically demanding limit its effectiveness as a screening modality for BCVIs.14

M U L T I D E T E C T O R  C O M P U T E D  T O M O G R A P H I C  A N G I O G R A P H Y  ( M D C T A )

Multidetector computed tomographic angiography (MDCTA) has emerged as a very convenient and effective screening tool for BCVI,15-19 especially after the advent of multidetector computed tomography (MDCT), with some studies reporting a sensitivity and specificity approaching that of DSA. In multitrauma patients, MDCT is routinely utilised to screen for injuries of the head, neck, spine, chest, abdomen and pelvic injuries. A MDCTA protocol to screen for BCVIs in high-risk patients is conveniently performed at the same time. It is also less expensive and non-invasive compared to DSA.14

In the literature, there only two prospective studies comparing single-slice computed tomographic angiography (CTA) and magnetic resonance

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**Table 2: Screening criteria for blunt cerebrovascular injuries**

<table>
<thead>
<tr>
<th>Denver Criteria</th>
<th>Memphis Criteria</th>
</tr>
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<tbody>
<tr>
<td>Signs/symptoms</td>
<td></td>
</tr>
<tr>
<td>Arterial haemorrhage or expanding haematoma</td>
<td>Cervical spine fracture</td>
</tr>
<tr>
<td>Cervical bruit</td>
<td>Neurological exam not explained by brain imaging</td>
</tr>
<tr>
<td>Focal neurological deficit</td>
<td>Horner’s syndrome</td>
</tr>
<tr>
<td>Neurological exam inconsistent with head computed tomography (CT) findings</td>
<td>Le Forte II or III fracture pattern</td>
</tr>
<tr>
<td>Stroke on follow-up head CT</td>
<td>Basilar skull fracture with involvement of the carotid canal</td>
</tr>
<tr>
<td></td>
<td>Neck soft tissue injury (seatbelt sign or hanging or haematoma)</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
</tr>
<tr>
<td>Le Forte II or III fracture pattern</td>
<td></td>
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<tr>
<td>Cervical spine fracture</td>
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<tr>
<td>Basilar skull fracture with involvement of the carotid canal</td>
<td></td>
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<tr>
<td>Diffuse axonal injury with Glasgow Coma Scale ≤6</td>
<td></td>
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<tr>
<td>Near hanging with anoxic brain injury</td>
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</tbody>
</table>

Source: Arthurs, et al.2
angiography (MRA) to DSA which were done by the Denver and Memphis groups. In their studies, CTA had a sensitivity of 47–68% and a specificity of 67–99%. CTA missed 55% of Grade I, 14% of Grade II, and 13% of Grade III injuries. The authors concluded in this study that CTA should only be used to diagnose BCVIs when DSA is not available. However, it is important to note that the CTA scanners used at that time were single slice CTAs, which along with other limitations such as timing contrast injection, image acquisition protocols, post-image processing delays (reformatting process), and inexperience with interpretation, might have accounted for the disappointing results in these two studies.

In 2003, 16-slice MDCTs were widely available across the USA and so trauma surgeons found resistance to using DSA. In a study by Berne et al. in 2004, 486 patients, identified to be at risk of BCVIs, underwent CTA. Patients who had a negative study received no further cerebrovascular imaging and were monitored for cerebral ischaemic complications. Patients who had a positive CTA underwent DSA to confirm the findings. The results showed that CTA had a sensitivity of 100% and a specificity of 94.0% and none of the patients who had a negative CTA subsequently developed any ischaemic neurological events. These results were questioned because the patients who had a negative CTA were not confirmed to be true negatives by DSA. In the same year, Bub et al. published a retrospective analysis that included 32 patients who were suspected to have BCVIs and underwent both MDCTA and DSA. Results showed that 17 BCVIs were identified in 15 of the 32 patients. MDCTA done by three different radiologists had a sensitivity of 83–92% and specificity of 88–98% for detecting BCIs. However, the sensitivity for vertebral artery injuries ranged from 40–60%, and the specificity ranged from 90–97%. In 2006, three studies, published by three different institutes, produced very similar results with regard to the use of 16-slice MDCT to scan for BCVIs in high risk patients. All three groups found MDCT to be as accurate as DSA in detecting BCVIs, with the exception of one patient in the study done by Eastman et al., where a Grade 1 injury was missed by MDCT and was detected by DSA. In all three studies, none of the patients who were initially found to have a negative CTA later developed complications attributable to an undetected BCVI.

Although many of the studies discussed above do prove that the accuracy of CTA approaches that of DSA, the lack of prospective data comparing 16-slice CTA to DSA and the small number of patients included in each study limit the reliability of the results and the validity of the conclusion that CTA is equivalent to DSA. It is recommended that patients who are at high risk for BCVIs should be considered for DSA regardless of their CTA findings, until a large, multicentre prospective trial proves the case.

MAGNETIC RESONANCE ANGIOGRAPHY (MRA)
The advantage of MRA over MDCT is the fact that it does not carry the risk of ionising radiation or the use of contrast, but in a multi-trauma setting MRA is not really a feasible or practical option. The time needed for the patient to be taken to the MR suite, for the test to be performed and the number of personnel required to perform the study are all limitations to its accessibility in a multi-trauma setting. However, in two prospective analyses by the Denver and Memphis groups, which compared CTA and MRA to DSA in patients suspected to have BCVIs, MRA had a sensitivity of 50–75% and specificity of 67–100%.

SONOGRAPHY
Duplex ultrasound is a portable and inexpensive tool that is well established in monitoring and diagnosing non-traumatic cerebrovascular pathology. However, the fact that it is operator dependant, has a limited ability to visualise cerebral vasculature at the base of the skull and also to visualise minimal injuries and dissections that are not associated with disrupted flow, has limited its role in detecting BCVI. In the few studies performed to evaluate the accuracy of duplex ultrasound to detect BCVIs, results were disappointing, showing that duplex has a low sensitivity and specificity compared to DSA and that it missed injuries in patients who later on developed ischaemic complications attributable to these injuries.
Management

The early detection and treatment of BCVIs has been shown to reduce the morbidity and mortality related to these injuries. Both symptomatic and asymptomatic patients with BCVI should be managed and closely monitored for any neurological deterioration. The optimal treatment of patients with BCVI is not yet well established. The appropriate management of BCVI depends on the specific injury and its anatomic site. Controversies do exist in the management of dissection, thrombosis and pseudoaneurysm formations. Older studies prefer surgical over non-surgical management of dissection and thrombosis. However, most of these lesions extend beyond the skull base, and are therefore not amenable to open surgical repair. In addition, most neurologic sequelae of these injuries are related to acute thrombosis, thrombus propagation and distal embolisation, making surgical reconstruction irrelevant. There is therefore growing support for nonsurgical management of dissections and thromboses. Prospective trials comparing surgery with anticoagulation are not feasible.

ANTICOAGULATION THERAPY

Although its efficacy has not been proven, anticoagulation therapy has been considered the treatment of choice in patients with BCVI, especially for those with high located intimal flaps, extensive dissections and small inaccessible pseudoaneurysms. Anticoagulation is documented to prevent cerebral embolisation and to avoid permanent occlusions of injured vessels. and have suggested improvement of outcomes with anticoagulation alone.

Initial systemic heparin therapy is safe and should be considered if no contraindications are present, or if the anticipated benefit outweighs the risk of bleeding in high risk patients. This should be followed by oral anticoagulation therapy with warfarin (Coumadin) for three to six months. Reported complications of anticoagulation include intracranial haemorrhage, gastrointestinal bleeding, retroperitoneal haemorrhage, bleeding at the site of blunt solid organ injury and re-bleeding from surgical wounds. These complications are reported to occur in 25–54% of trauma patients.

Most authors agree on the need for follow-up for patients treated initially with anticoagulation for their BCVI in order to detect any subsequent development of pseudoaneurysms requiring surgical or endovascular interventions.

ANTIPLACEBOTS THERAPY

Aspirin (and in few other reports, clopidogrel) has been used as an alternative to heparin in the treatment of patients with BCVI. It has been shown to have similar efficacy to heparin in preventing neurological events. In fact, aspirin has been proven to have a better safety profile with less risk of bleeding compared to heparin, especially in the population of trauma patients. A combination therapy of anticoagulation and antiplatelets has been practised, but any advantage has not been proven; it definitely requires further prospective trials to elicit any added benefit to the single therapy.

OPEN SURGICAL REPAIR

Direct surgical repair is advocated for discrete lesions at the carotid bifurcation or lesions below the base of the skull making it amenable for proximal and distal control. Most of the time, open surgical repair is rarely considered for patients with BCVI for the reasons mentioned above. Management of pseudoaneurysms is less controversial and most authors recommend surgical repair whenever it is technically feasible. Small or inaccessible pseudoaneurysms have been managed by anticoagulation with or without proximal ligation, or by the rarely used extracranial-intracranial bypass.

ENDOVASCULAR THERAPY

With the development of the less invasive endovascular techniques, most carotid pseudoaneurysms and dissection flaps that result from BCVI have been managed successfully with angioplasty and endoluminal stenting. Endovascular therapy is an alternative to open surgical repair and of great value in the distal carotid lesions which are not amenable for open surgical repair. This therapy is recommended in cases where there is a contraindication for anticoagulation. Bare or covered stents, either balloon expandable or self-expanding, have been used extensively with good outcome and no further neurological events reported. As compared to data on peripheral stenting, antiplatelets
therapy (aspirin and clopidogrel) is advised after endoluminal stent therapy to prevent stent thrombosis and embolic ischaemic events. Balloon occlusion techniques are a well established mode of treatment for carotid-cavernous sinus fistulae, and the results are fair to good.

Outcome

The prognosis of BCVI is generally poor. All reported cases of complete arterial disruption have been fatal. Other injuries of dissection, thrombosis and pseudoaneurysm formation carry variable outcomes depending on the site of the injury as well as the time of detection of these injuries. Mortality rates after BCVI have been reported to be 5–40% and reasonable neurologic recovery in only 20–60% of all survivors. Although there is some evidence to show improved outcomes with anticoagulation and antiplatelets therapy and in selected cases of surgical and endovascular interventions, the outcome of BCVI depends more on the speed of diagnosis. A high index of suspicion and the maintenance of aggressive evaluation protocols for patients with possible BCVI will definitely avoid diagnostic delay and may improve the overall outcome.

Conclusion

Blunt cerebrovascular injury (BCVI) may be overtly present in more than 1% of patients with blunt trauma. Aggressive screening strategies uncover injuries in up to 44% of those screened. If not appropriately diagnosed and treated in a timely manner, many such injuries are responsible for significant morbidity and mortality. Aggressive screening protocols are now feasible using newer generation, multidetector helical scanners capable of detecting small intimal defects in a relatively non-invasive manner.

Treatment has focused on reducing the atheroembolic tendency of the disrupted vessel wall. Anticoagulation with heparin and antiplatelet agents has been used; however, in a multitrauma patient, the risks of bleeding and the need for immediate surgery must be taken into account. Certain injuries to cervical vessels may be amenable to endovascular therapy. Therefore a multi-disciplinary team consisting of the emergency physician, trauma surgeon, vascular surgeon, interventional radiologist and intensivist is recommended for immediate and follow-up care. A high index of suspicion and maintaining aggressive evaluation protocols for patients with possible BCVI will definitely avoid diagnostic delay and may improve the overall outcome after BCVI. Further research into optimal treatment strategies is warranted.

References


Umbilical Cord Blood Banking and Transplantation
A short review

Salam Alkindi1 and David Dennison2

Abstract: It is more than 20 years since the first cord blood transplant (CBT) was performed, following the realization that cord blood (CB), which is normally wasted, is rich in progenitor cells and capable of rescuing haematopoiesis. Since then it has been appreciated that CB is rich in stem cells, and has many other features not least of which is its ability to rescue the transplanted patient without a rigid need for full human lymphocyte antigen (HLA) compatibility. Also it is easily accessible, relatively free from infections and poses no medical risk to the donor. However, the quantity of the stem cells is rather small, thus predominantly restricting its use to children or adults requiring double units. In Oman, we have taken a keen interest in stem cell research and also CBT.

Keywords: Umbilical cord blood; Cord blood transplantation; Cord blood stem cell; Cord blood banking; Private cord blood bank; National cord blood bank.

It is about 20 years since the first cord blood transplant (CBT) was performed in a young patient with Fanconi's anaemia. Since then, due to technological advances, there has been a tremendous progress in the utilisation and application of CBT, both in terms of quantity and quality.1

The use of CBT has risen following the understanding that cord blood (CB), which is normally wasted following delivery of a baby,
Umbilical Cord Blood Banking and Transplantation
A short review

contains large quantities of pluripotential stem cells that could be utilised to regenerate or rescue haematopoietic stem cells (HSC), following their exposure to accidental or therapeutic ablative therapy. Pleuripotent stem cells are undifferentiated cells that are capable of dividing, self-renewal, and generating progeny of highly specialised cells, upon exposure to optimal environmental stimuli in what is termed a bone marrow microenvironment.2,3 This microenvironment is under the influence of various biomolecules, with interplay between adhesions molecules, cytokines and their receptors.3

The stem cells found in CB are also similar to those found in the bone marrow and are responsible for the regenerative capacity of the bone marrow’s haematopoietic activities. The initial experiments centered on a severe combined immune deficiency (SCID) mouse model that could be rescued by giving these stem cells. The progress that was made in this area was paralleled by progress in the ability to define these stem cells through the process of antibody labelling using flowcytometry, combining both functional and phenotypic assays.4

More recently, the focus has also been on the stromal support cells as they are found to play a crucial role in maintaining the integrity of the haematopoietic cellular milieu.5 These cells originate from mesenchymal stem cells that are not only necessary for the integrity of other marrow stem cells, but are capable of giving rise to many tissue types including cartilage, fat, muscle and bones.5,6 Subsequently, it has been demonstrated that cord blood units (CBU) have a number of features which makes them a highly favourable source of stem cells in the ever expanding range of stem cell therapy. Having realised the potential uses of CBUs, it was deemed necessary to establish cord blood banks (CBBs) in order to collect and store these units until the need for them arose.

Advantages of Cord Blood Transplants

A CBU contains a large number of progenitor cells that can be used to transplant most paediatric and some adult patients who require this form of therapy. These units have a low risk of viral infection (although this is not completely eliminated as Epstein-Barr virus [EBV] cases has been reported), in particular from cytomegalovirus [CMV].7 Moreover, CBUs are accessible and secured, so that they could be used at any time. This means that CBU units are ready for use when the recipient is ready for them, and so the transplant can be scheduled at the convenience of the recipient (patient) and not that of the donor. Furthermore, it is also known that the incidence of graft-versus-host disease (GVHD) is lower compared with bone marrow or peripheral blood transplantation. This may be related to the immaturity of the immune system at birth and the decreased potential of alloreactive lymphocytes.8 As a result, it is not strictly necessary to have a complete HLA match in CBU selection compared to peripheral blood or bone marrow selection. At the same time, the graft-versus-leukaemia (GVL) effect is maintained, fulfilling one of the main purposes of any allogeneic stem cell transplant procedure. Additional advantages, include zero risk to the donor since this blood is normally not used and wasted [Table1].

Disadvantages of Cord Blood Transplants

There are, however, some obstacles to the widespread use of CBU [Table 2], including the sometimes small number of stem cells in each unit, which leads to a delayed engraftment, and may be reflected in the increased transplant related mortality/morbidity and reduced survival. This is
Salam Alkindi and David Dennison

### Table 2: Disadvantages of cord blood transplantation

<table>
<thead>
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<th>Disadvantages</th>
<th>Consequences</th>
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<tr>
<td>Reduced cell dose</td>
<td>May delay engraftment/ reduce survival</td>
</tr>
<tr>
<td>Units may be small</td>
<td>Large adult recipients (≥60 Kg) require two units</td>
</tr>
<tr>
<td>Haematologic and immunologic disorders may not be apparent at birth</td>
<td>Requires careful donor screening and testing for common hereditary blood and immune disorders</td>
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Probably the most important limitation in CBT. Furthermore, since these units are small, (with reduced volume and quantity of stem cells), they may not be sufficient for large patients, although this could be augmented by using two human lymphocyte antigen (HLA) matched units at the same time. Efforts are being made to enhance the number, potency and engrafting capabilities of the collected stem cells through ex-vivo and in vivo manoeuvres, by modulating the microenvironment, cell receptors, and signalling pathways that control them.5

There are also efforts to enhance engraftment, including enhancing homing of the transfused cells as well as direct intra-bone marrow injections.10,11 The stored unit is not known for any severe haematologic or immune disorders, which may be transferred by the transplant process, and only for this reason, the donor is examined carefully after 6 months and the unit is also tested for haematologic and immune deficiency syndromes which may manifest only in the adult life. Extensive testing for common hereditary disorders, although very relevant to a country such as Oman, would be quite expensive, and the predictive value of such tests could be improved by taking a detailed family history from the parents.

Despite all of the above difficulties, CBT is growing, and CBU storage is rising worldwide. The increasing interest in CBU has therefore necessitated the need for CBBs of which there are currently two types.

## National Voluntary Cord Blood Banks

National voluntary CBBs generally cater for mothers who have children with a disease that is cured by bone marrow transplant (BMT) such as thalassaemia, sickle cell disease or leukaemia. In these cases, mothers are encouraged to collect their babies’ CB for possible future related umbilical CBT. These CBUs are collected and a process of HLA matching is done. It is also now possible in some centres to make a selection of disease-free offspring and HLA-matched babies as part of preimplantation genetic determination (PGD).12 Parents also can elect to donate the CBU of their baby to the national CBB to be used for patients where donors could not be found from their own family, allowing many matched but unrelated CBTs to be performed. With the average family size declining in the Western world, it is estimated that only about 25% of Caucasians will have a fully matched unrelated donor, and CBT has become in this regard an attractive source of stem cells.13 Recent statistics suggest that more than 400,000 CBU units are stored in banks in about 40 countries worldwide for use in unrelated transplants; of these, around 20,000 CBUs have been used for transplant so far worldwide, contributing to the cure of many children with haematological malignancies and bone marrow failure disorders who do not have matched family donors.14 Interestingly in fact, CBT has become more popular, particularly in children, and in 2009 more unrelated CBTs were performed than unrelated BMTs worldwide.15,16 Public banks store CBUs free of charge, samples are used to treat any patient without a donor and these banks are financed by public money.16

![Figure 1: Indications for bone marrow transplantation, Sultan Qaboos University Hospital, Oman, June 1995 to Oct 2010.](image-url)
Private Cord Blood Banking

Upon requests from interested parents, CBUs are also collected for personal use of that newborn in the future and, although the odds ratio for their utilisation has risen with time, it remains between 1 in 25,000 to 1 in 200,000 in the first 20 years of life.\textsuperscript{17} This has resulted in the proliferation of private (for-profit) CBBs that store these units. Their number is rising worldwide, capitalising on the idea that CB usage is expanding daily, beyond the currently available indications. These banks charge a fee to store CBUs exclusively for that neonate’s family only and only this family may access them. There are about 900,000 CBUs stored in private banks and more than 100 reports of successful autologous CBTs done worldwide by this method. Although the use of such CBUs for non-malignant conditions is reasonable, their use for the treatment of malignant conditions such as leukaemia will be limited by the lack of GVL—one of the main reasons for having allogeneic transplants. Caution has to be exercised in unrestrictedly advocating the widespread use of such banks, one of the many reasons being the limited future clinical utility of CBUs; for example, the European Group for Blood and Marrow Transplantation (EMBT) reported 544 cord blood transplants in 2006, but none of them was autologous.\textsuperscript{18}

Furthermore, the professional reluctance to accept private CBBs stems from the fact that the amount of total nucleated cells (TNC) in these units is small allowing at most only paediatric transplants. It is also possible that these CBUs are contaminated with leukaemogenic cells prohibiting the most important indications for cord transplant in childhood leukaemia.\textsuperscript{19} The yield of CBUs as well as their utilisation for mesenchymal stem cell therapy remains controversial.\textsuperscript{20} Arguments for lack of support for private (for profit) banks from academic and scientific community, rest on the lack of clinical justifications for autologous banking, poor quality standards regarding collection and storage, no guarantees in case of bankruptcy and misleading advertising from CB companies.\textsuperscript{20} Recent studies from European countries suggest a strong preference for public CBB as opposed to private blood banking.\textsuperscript{16,19} Hybrid banks are also gaining popularity, where companies are collecting units for a fee for a private family use, and at the same time collect units for national use. This enables local health authorities to cover some of the costs of storing these public units.\textsuperscript{19}

What are the Indications for Cord Blood Transplantation?

CBUs contain a large number of stem cells that could be used in transplanting many diseases including

\begin{figure}[h]
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\includegraphics[width=\textwidth]{Figure2.png}
\caption{Bone marrow transplantation for hereditary blood disorders at Sultan Qaboos University Hospital, Oman, June 1995 to Oct 2010.}
\end{figure}
stem cell transplantation (bone marrow [BM], peripheral blood [PB] and CB), has been carried out at Sultan Qaboos University Hospital since 1995. Although the start was modest in terms of numbers, over the years more has been achieved, and results are now comparable with the best transplant centres worldwide. Currently, having done over 200 transplants of BM, PB, and CBT for leukaemia, myeloma, lymphoma, hereditary blood disorders and immune deficiency syndromes, the programme is gaining strength. Diversification was achieved in the programme by the use of BM, PB, and CB both in related and, more recently, unrelated donors, as well autologous transplantations. The programme aims to address the unique disease distributions seen in our country by catering for transplants in haemoglobin disorders such as thalassaemia and sickle cell disease, as well as immune deficiency syndromes, and malignant disorders such as leukaemia, lymphoma and myeloma. Furthermore, for successful stem cell transplantation, traditionally a full myeloablative conditioning therapy using chemotherapy, radiotherapy or both has been used. This helps to create a less hostile BM environment, eradicates any residual abnormal clone and suppresses the recipient’s immune response. However, more recently we have started reduced intensity conditioning transplantations (RIC) allowing us to include older patients with malignant conditions as well as more complicated patients with non-malignant disease such as SCD patients. RIC, particularly in SCD, has been used following the understanding of improved survival of healthy donor erythrocytes as compared to the recipient abnormal cells. Furthermore, as ineffective erythropoiesis lends a competitive advantage to donor erythroid progenitors, this creates a mixed donor/recipient chimera to co-habilitate together first. Later the donor clone eventually dominates and replaces the recipient’s original clone. RIC has also allowed many patients who could not tolerate a fully myeloablative therapy to have a stem cell transplant, allowing appropriate disease control with acceptable transplant related morbidity/mortality.27

The spectrum of the conditions that we have treated in our centre is shown in Figure 1, whereas Figure 2 outlines in detail the transplantations for hereditary blood disorders and is reflective of pattern of diseases that are prevalent in Oman. Our CBB was established as the first national CBB in the country to cater for parents who have a child suffering from one of the disorders that are cured by BMT and who wanted their newborn baby’s CBU to be collected and processed for possible matched related transplant for their offspring. We have also created a voluntary CB banking system for those who want to donate their baby’s CB to our national CBB. Having obtained local ethical approval, our counsellors approach expectant mothers and their partners in the antenatal clinic for consent to collect cord blood. This is then collected by trained midwifes in the delivery ward, and undergoes red cell depletion at our stem cell processing laboratory. Samples are taken for HLA typing, serology for hepatitis and HIV as well as microbial cultures. Also the sample undergoes cell counts and, in related (sibling) cord samples, any count is acceptable; however, in voluntary cord blood samples, only units with total nucleated cells above $6 \times 10^8$/kg are cryopreserved, other units being discarded.28 So far we have collected cord blood from 81 siblings and >40 unrelated CB units. The number of the frozen CBUs is increasing and our aim is to establish a fully fledged CBB according to the international regulations of the Foundation for Accreditation...
Conclusion

Stem cells derived from CB, BM, and PB are contributing significantly to the curative treatment potential available for many acquired and congenital disorders in Oman and worldwide. National CBBs remain the preferred option, on economic, scientific and ethical grounds, until there are further advances in knowledge on the use of autologous CBT. Our strategy is to make stem cell therapy accessible to our patients, employing well established procedures for stem cell collection, storage, in vitro expansion and manipulation in order to achieve a successful national, culturally accepted CBB.

References


Neonatal Screening
Mean haemoglobin and red cell indices in cord blood
Omani neonates

Salam Alkindi,1 Anil Pathare,2 Ali Al-Madhani,3 Shaoha Al-Zadjali,4 Hamood Al-Haddabi,2 Qamariya Al-Abri,5 David Gravell,4 Mariam Mathew,4 Rajagopal Krishnamoorthy3

The aim of this study was to validate the interpretation of red blood cell indices in newborn cords of Omani neonates. Mean haemoglobin and red cell indices in cord blood from 7,837 newborns, were analysed with full blood count and Hb level. Additionally, in cases with HbA <10%, the β-globin gene was directly sequenced for Omani neonates. No case of HbH was detected. In the former subgroup respectively, the mean Hb (14.79±11.80 pg), mean corpuscular volume (MCV) (107.66±7.55 fl), and mean corpuscular haemoglobin concentration (MCHC) (37.3±4.07) pg, were observed. In the latter subgroup, respectively, the mean Hb (3.70±3.44 g/dl), red cell distribution width (RDW) (17.01±17.01%) and mean corpuscular haemoglobin (MCH) (10.96±10.96 pg) were observed. DNA sequencing of samples with abnormal HbA was performed to identify the cause of abnormal HbA. The cause of abnormal HbA was Thalassaemia in 7.40% cases (7.40±5.05%) and in 92.59% cases (12.04±11.38%), it was normal.

Abstract: Objectives: The aim of this study was to validate the interpretation of red blood cell indices in complete blood count (CBC) and high performance liquid chromatography (HPLC) results on cord blood samples in consecutive Omani neonates. Methods: Cord blood samples from 7,837 neonates, were analysed with CBC and HPLC using the β-thalassaemia short programme. Direct sequencing of abnormal samples with HbS, HbD, HbE and HbC was performed to validate the HPLC results. Additionally, in cases with HbA <10%, the β-globin gene was directly sequenced for β-thalassaemia mutation analysis. Results: Overall, 4,042 subjects (51.58%) had normal HPLC (HbA2 22.88±8.03; HbA2 77.02±8.04), whereas the presence of Hb Barts in the remaining 3,795 cases (48.42%) indicated the presence of α-thalassaemia. No case of HbH was detected. In the former subgroup respectively, the mean Hb (15.38±3.44 g/dl), red cell distribution width (RDW) (17.01±17.01%) and mean corpuscular haemoglobin concentration (MCHC) (30.98±3.44 g/dl) were observed. In the latter subgroup respectively, the mean Hb (14.79±2.90 g/dl), and mean corpuscular haemoglobin concentration (MCHC) (30.98±3.44 g/dl) were observed. DNA sequencing of samples with abnormal HbA was performed to identify the cause of abnormal HbA. The cause of abnormal HbA was Thalassaemia in 7.40% cases (7.40±5.05%) and normal in 92.59% cases (12.04±11.38%).

CLINICAL & BASIC RESEARCH

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Several studies have shown that inherited haemoglobinopathies are widespread in Oman and are at a sufficiently high level to be of considerable national concern.\textsuperscript{1,2} Specifically, Oman has a relatively high prevalence of $\alpha$ and $\beta$-thalassaemia, G6PD deficiency and sickle cell syndromes compared to other Arabian Gulf Countries.\textsuperscript{3-6} A community based survey carried out in 1995 in Oman showed a significantly high prevalence of haemoglobinopathy.\textsuperscript{5} The reported prevalence of sickle cell trait was 6% and $\beta$-thalassaemia trait was 2%, whereas the prevalence of homozygous sickle cell and $\beta$-thalassaemia was 0.2% and 0.07% respectively. The prevalence of other abnormal haemoglobins namely HbD, HbE and Hbc were 0.6%, 0.3% and 0.02% respectively. Enzyme deficiency of G6PD was also prevalent (18%). Our own report in 2010 also showed comparatively high prevalence rates.\textsuperscript{8} It has been postulated that the likelihood of children being born with a major haemoglobinopathy in Oman would be about 3 per 1,000 births.\textsuperscript{5} Thus, with an annual birth rate of 35.76 births/1,000 population,\textsuperscript{3} there would approximately be 106 new cases every year. Therefore, with this burden of haemoglobinopathy, the establishment of neonatal reference ranges is extremely important.

This study was undertaken under the auspices of His Majesty’s Research directive to screen neonates by implementing a universal newborn screening at the Sultan Qaboos University Hospital (SQUH), Oman. Cord blood samples from newborns at SQUH (representing the Muscat Governorate), and from the Sohar Hospital (representing the Batinah coastal region) were collected.

The objectives of our study were twofold. The first objective was to screen the newborn Omani subjects to establish the current prevalence of haemoglobinopathy and to see the effect of the decade long measures that were implemented following the first community study in 1995. The second objective was to validate the CBC and HPLC interpretations of the cord blood red cell indices in the Omani neonate.

**Advances in Knowledge**

1. This study validates the cord blood red cell indices obtained from Omani newborn subjects without any underlying haemoglobinopathy.
2. It validates the cord blood red cell indices in Omani newborn subjects with $\alpha$-thalassaemia.
3. Finally, it validates the abnormal haemoglobins in Omani newborn subjects.

**Application to the patient care**

1. The results of this study will benefit patient care by comparative analysis of Omani cord blood red cell indices in subjects without any underlying haemoglobinopathy with those from other countries in the region.
2. It will improve patient care by comparative analysis of Omani cord blood red cell indices with $\alpha$-thalassaemia with those from other countries in the region.
3. It will also improve patient care by comparing the influence of $\alpha$-thalassaemia on cord red cell indices in the different subsets with variant haemoglobins amongst Omani newborn subjects.

**Keywords:** Neonatal; Screening; Reference range, Haemoglobin; Variants; Alpha-thalassaemia.
Table 1: Comparative analysis of cord blood red cell indices (mean ± SD) in newborn Omani neonates compared with Saudi neonates

<table>
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<tr>
<th>Haemoglobins</th>
<th>n</th>
<th>Hb gm/dl</th>
<th>RBC 10^6/L</th>
<th>HCT %</th>
<th>MCV fl</th>
<th>MCH pg</th>
<th>MCHC g/dl</th>
<th>RDW %</th>
<th>HbA %</th>
<th>HbF %</th>
<th>Ab. Hb S,D,E,C</th>
</tr>
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<tbody>
<tr>
<td>Omani HbAF</td>
<td>3,765</td>
<td>15.38</td>
<td>4.69</td>
<td>50.5</td>
<td>107.66</td>
<td>33.31</td>
<td>30.98</td>
<td>17.01</td>
<td>22.88</td>
<td>77.02</td>
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<td></td>
<td>2.04*</td>
<td>0.68*</td>
<td>7.18*</td>
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<td>8.03*</td>
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<tr>
<td>Saudi HbAF</td>
<td>243</td>
<td>15.1</td>
<td>4.5</td>
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<td>106.0</td>
<td>33.6</td>
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<td>27.2</td>
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Legend: * P <0.05 between red cell indices, with and without α-thalassaemia (Hb Bartts) in Omani neonates; RBC = red blood cell; HCT = haematocrit; MCV = mean cell volume; MCH = mean corpuscular haemoglobin; MCHC = mean corpuscular haemoglobin concentration; RDW = red cell distribution width; HbAF = Hb A+F; HbAFS = Hb A+F+S; HbFS = Hb F+S; HbAFD = Hb A+F+D; HbAFE = Hb A+F+E; HbAFC = Hb A+F+C.

Methods

This study was conducted under the auspices of His Majesty’s Strategic Research Project initiated and funded between the years 2005 to 2008. The study was approved by the Institutional review board and conforming to the Declaration of Helsinki. The study enrolled a total of 3,740 subjects from SQUH in Muscat and 4,097 neonates from Sohar Hospital, Oman. All data was archived in a Microsoft Excel database. Statistical analysis was performed using the student’s t test with a value <0.05 considered significant.

Between April 2005 and March 2007 and after informed consent was obtained, a total of 7,837 consecutive cord blood samples were...
screened prospectively, for the presence of possible haemoglobinopathies by a full blood count followed by HPLC using the Biorad Variant II β-thalassaemia short programme.

The CBC was performed using EDTA cord blood samples on Cell Dyn 4000™ automated blood cell counter (Abbot Diagnostics, Abbot Laboratories, IL, USA) within 4–12 hours of collection. HPLC was performed within 12–24 hours of collection using the β-thalassaemia short programme on the Bio-Rad VARIANT IITM instrument (Bio-Rad Laboratories, Hercules, CA, USA) using the manufacturer’s instructions and controls. The samples were refrigerated from the time of collection up to the time of analysis. All samples were then processed to isolate and store mononuclear leukocytes for subsequent confirmatory molecular diagnostics.

Direct sequencing of abnormal samples with HbS, HbD, HbE and HbC was performed on the ABI Prism™ 3100 genetic analyser (Applied Biosystems, Foster City, CA, USA) to assign the genotype status to these subjects and validate the HPLC results. The DNA sequencing was performed by polymerase chain reaction (PCR)-amplified β-globin gene segment to look for the following mutations, namely HbS (β^6 Glu-Val), HbD (β^121 Glu-Gln), HbE (β^26 Glu-Lys) and HbC (β^6 Gln-Lys) as per the manufacturer’s instructions and PCR conditions. Additionally, in samples with HbA below 10%, the β-globin gene was directly sequenced including the promoter, all exons and introns in these samples to look for all the known mutations reported for β-thalassaemia.

Results

On the basis of a CBC and HPLC, all samples were characterised as either normal (HbA+HbF), 4,042 cases; or α-thalassaemia, (HbA+HbF+Hb Barts) 3,795 cases. In the former group, 200 cases also had HbS, 45 cases had HbD, 29 cases had HbE, and 3 cases had HbC. Whereas in the latter group, 229 cases additionally also had HbS, 28 cases had HbD, 30 cases had HbE, and 3 cases had HbC.

Table 1 shows the comparative analysis of cord blood red cell indices (mean ± standard deviation [SD]) from newborn Omani neonates compared with Saudi neonates.8 In a subset of the Omani neonates without any abnormal haemoglobin (HbA+HbF) (n = 3,765), the mean (±SD) Hb(g/dl), RBC count (x 10^12/L), haematocrit (Hct) (%), mean cell volume (MCV) (fl), mean corpuscular haemoglobin (MCH) (pg), mean corpuscular haemoglobin concentration (MCHC) (g/dl), red cell distribution width (RDW) (%), were 15.38±2.04; 4.69±0.68; 50.5±7.18; 107.66±7.75; 33.31±4.07; 30.98±3.44, and 17.01±2.17 respectively. Whereas in the subset of subjects with HbA, HbE, Hb Barts (n = 3,505), the study observed a 48.42% incidence of α-thalassaemia, based on low MCV and MCH on the CBC and significant amounts of Hb Barts on HPLC based on the manufacturer’s cut-off limit. Their mean (±SD) Hb(g/dl), RBC count (x 10^12/L), Hct (%), MCV (fl), MCH (pg), MCHC (g/dl), RDW (%), were 14.79±2.90; 5.09±0.77; 107.66±7.75; 33.31±4.07; 30.98±3.44, and 17.01±2.17 respectively. There was a statistically significant reduction in the MCV, MCH, MCHC, HCT, Hb and an increase in the RBC count. Furthermore, MCV was the best discriminator between the two
Neonatal Screening
Mean haemoglobin and red cell indices in cord blood from Omani neonates

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Table 3: Reference range for various haemoglobins (%) in cord blood from newborn Omani subjects (n = 7,837)

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<th>HbS % (n = 429)</th>
<th>HbD % (n = 73)</th>
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Population reference range for various haemoglobins (%) in cord blood from newborn Omani subjects (n = 7,837) are shown in Table 3. The mean HbA, HbF, HbS, HbD, HbE, HbC (±SD) were 22.88±8.04; 77.02±8.04; 13.6±6.96; 8.88±4.87; 6.64±2.98, and 6.21±3.41 respectively. The overall incidence of other haemoglobinopathies was 9.86% (n = 773), with 5.46% (n = 428) incidence of sickle haemoglobin.

Discussion
Oman is a country with a population comprising a wide range of ethnic groups, and high rates of consanguinous marriages. This is a significant reason for the increased prevalence of haemoglobinopathies, which is of growing importance as knowledge of the population structure can be a unique aid in planning genetic services.

HPLC is a powerful tool to screen newborns for haemoglobinopathies. Cord blood sampling offers an easy, simple and practical method for demonstrating the coexistence of α-thalassaemia by detecting the presence of Hb Barts. We were able to identify these subjects very well with the Biorad Variant II© system, using the β-thalassaemia short programme which works on the principle of cation exchange high pressure liquid chromatography. Since each haemoglobin has a characteristic retention time, Hb Barts being a fast moving haemoglobin, is easily separated and eluted from the other haemoglobins present in the neonatal cord blood samples. The precision is further improved by running a chromatographic calibrator with an assigned value for Hb Barts at the beginning of each run. Thus, using the presence of Hb Barts as an indicator of α-thalassaemia, we found that 51.57% subjects had normal HPLC (absence of Hb Barts).

Before the availability of molecular diagnostic methods for the diagnosis of α-thalassaemia, there was good evidence that the presence of Hb Barts in the neonatal period indicated the presence of α-thalassaemia. However, the relationship between the amounts of Hb Barts and the underlying molecular defect was not clear. Most surveys using assays that detect 0.5% to 1% Hb Barts in cord blood detect a large proportion of neonates with α-thalassaemia, but not all; hence, surveys solely based on the presence of Hb Barts in cord
blood consistently under-reported the frequency of α-thalassaemia. Moreover, although the levels of Hb Barts are related to the degree of α-chain deficit, there is no way to distinguish the various α-thalassaemia syndromes solely on the basis of HPLC.

A comparative analysis of the red cell indices in these two groups revealed that α-thalassaemia resulted in a lower mean Hb, Hct, MCV, MCH, MCHC and HbF whereas it resulted in a higher mean red cell count and HbA concentration [Table 1]. Furthermore, all these differences were statistically strongly significant. The best discriminator was found to be MCV followed by red cell count, MCH and Hb concentration. Similar observations have been also made by other investigators; however, the degree of abnormality varies amongst these parameters.

In subjects with HbD, the presence of α-thalassaemia also resulted in lower HbA, HbD, MCV, and MCH; whereas the Hb, red cell count, Hct and HbF were higher. The differences in RBC count, MCV and HbF were statistically significant [Table 1].

In subjects with HbE the presence of α-thalassaemia resulted in lower HbA, HbE, MCV, MCH, Hb, RBC counts and Hct, whereas only the HbF was higher [Table 1]. The differences in Hb, MCV and HbF were statistically significant.

Overall, α-thalassaemia appears to influence all the red cell indices when it is the only abnormality. In the presence of abnormal haemoglobin, its influence was marginal unless the abnormal haemoglobin was present in a homozygous state, as in subjects who showed homozygous HbS. Thus with the presence of α-thalassaemia leading to a reduction in α-chains, the additional presence of a β structural variant will lead to a variable situation the outcome of which depends on the net globin chain synthesis rate. Some β-globin variants like HbE are synthesised less efficiently than HbA and represent less than 50% of the haemoglobin in the heterozygote. Furthermore, the rate of assembly of the αβ-chain complexes also would affect the final product. Therefore, the formation of the αβ-dimer is the rate limiting step in the assembly of haemoglobin.

**Figure 1:** Capillary electropherogram results of DNA sequencing by PCR-amplified β-globin gene segment to document HbS (β6 Glu-Val) (a,b), HbD (β121 Glu-Gln) (c), HbE (β26 Glu-Lys) (d), HbC (β6 Glu-Lys) (e), HbA (β6 Asp-Val) (f), HbS (β121 Glu-Gln) (g), and the common β-thalassemia mutations (h).
Direct sequencing of samples with abnormal haemoglobin was used to validate the interpretation of the CBC and HPLC results and was found to be quite accurate [Figure 1]. All cases with HbD, HbE, HbC were documented to show HbD (β121 Glu-Gln), HbE (β26 Glu-Lys) and HbC (β6Glu-Lys) mutation respectively. All cases with HbS were shown to carry the HbS (β6 Glu-Val) except in one case which had the delta chain codon 16 mutation, and is known to show a small abnormal haemoglobin band in the HbS window on HPLC in the β-thalassaemia short programme HPLC runs. Furthermore, in cases with low HbA (below 10%), 98.1% of subjects were documented to have one of the known mutations described as causative of β-thalassaemia, consistent with the recommendations of the manufacturer (Bio-Rad Laboratories, Hercules, CA, USA).

Thus, the significantly high prevalence of haemoglobinopathies in newborns from Oman emphasises the value of neonatal cord blood screening. This should be implemented as the first step in the national strategy towards total management of haemoglobinopathies—including early diagnosis, comprehensive clinical care and counselling of the affected families. In the light of the results of the current study, this initiative is being taken forward to encompass all the regions of Oman. The results of this large study would indicate that using HPLC is a cost effective method (<2 US $ per sample).18

Conclusion

In this study, for the first time, we were able to establish and validate the neonatal cord blood red cell indices and the prevalence of underlying abnormal haemoglobin by a universal newborn cord blood screening in the Omani population. The study observed that approximately 10% of the population still carries an abnormal haemoglobinopathy with significant clinical consequences, like Hb S, Hb D, Hb C and the β-thalassaemia gene. Furthermore, we have also established the prevalence of α-thalassaemia in this cohort and its potential to alter the red cell indices as well as its ameliorating effect when co-associated with the presence of other haemoglobin variants, which are highly prevalent in Oman. The comparative analysis of cord blood red cell indices and mean haemoglobins showed similar results to those seen with neonates from other countries in the region.

Therefore, as a direct result of this study, it is suggested that “targeted screening” with prescreening of both parents, and then selecting only the samples of neonatal cord blood from newborns with one parent having an underlying genetic trait for haemoglobinopathy, would result in a huge cost saving compared to the universal neonatal cord blood screening undertaken in this study.

CONFLICT OF INTEREST

The authors reported no conflict of interest.

ACKNOWLEDGEMENTS

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References


Simultaneous Detection of Dengue NS1 Antigen, IgM plus IgG and Platelet Enumeration during an Outbreak

*Subhash C Arya, Nirmala Agarwal, Satibh C Parikh, Shekhar Agarwal

ABSTRACT: Objectives: During 2010, there was an increase in dengue virus infections in New Delhi, India compared to 2009. This study was conducted at Sant Parmanand Hospital during this outbreak to determine the utility of a ‘Dengue Package’, comprising simultaneous detection of dengue non-structural protein 1 (NS1), anti-dengue IgM, anti-dengue IgG and platelet enumeration for early diagnosis, better case management and faster public health response. Methods: Blood samples were tested for Dengue NS1, IgM and IgG using the single-step immunochromatographic One-step dengue NS1 Ag and IgG/IgM test, while platelets were enumerated with automatic analysers yielding results within 1–2 hours. Results: Of the 1,886 patients screened with the ‘Dengue Package’, 678 were NS1-positive and 1,208 were NS1-negative respectively, in different combinations. In 394 cases, NS1 was exclusively positive while 29 were also IgG positive. In 942 cases NS1, IgM and IgG were negative (triple negative). The platelet counts in the NS1 positive cases were lower than the NS1 negative cases, mean and standard deviation (SD) 116.8±70.2 x 10⁹/L; 95% confidence interval (CI) 66.6–74.1 and 167.2±94.0 x 10⁹/L, P=0.0001. Platelet counts were <20 x 10⁹/L in 20 NS1 antigen-positives and 42 NS1 antigen-negatives. Conclusion: During the outbreak, swift availability of the ‘Dengue Package’ assisted patient management, platelet transfusions, implementation of anti-vector measures and public health notifications. Testing for NS1 assisted the diagnosis of an additional 22.4% cases; of these 394 evidence of primary infection and 29 of secondary infection. The ‘Dengue Package’ was useful in tackling the rise in suspected cases.
During the late incubation period, or initial phase of dengue virus infection, laboratory disease confirmation is through viral isolation in cell culture and/or molecular investigations, or immunofluorescence, or immunohistochemistry. The dengue virus non-structural protein non-structural protein 1 (NS1) that develops right at the beginning of the feverish period and before the appearance of dengue IgM and/or IgG is emerging as a suitable option for dengue diagnosis. Consequent to a multi-country evaluation of two commercially available NS1 enzyme-linked immunoabsorbent assay (ELISA) assays, a combination of NS1 and IgM detection in samples during the first few days of illness was recommended to increase overall dengue diagnostic sensitivity.

Platelet therapy is a standard clinical practice for dengue patients with severe thrombocytopenia. However, during introductory screening, a platelet count is not done in many cases. This results in delays in starting platelet therapy. During the 2010 spurt in the incidence of dengue in New Delhi, simultaneous screening for NS1, IgM and IgG and platelet enumeration was launched at the Sant Parmanand Hospital, a 140-bed tertiary care, multi-disciplinary, private hospital in Delhi which caters to populations in the national capital and adjoining townships. The study was aimed to assess the utility of a concurrent identification of NS1, IgM, IgG, and platelet counting offered as the ‘Dengue Package’ for patients, clinicians and community.

**Methods**

During the period August to November 2010, samples from 1,886 suspected dengue patients were taken for testing by the combined ‘Dengue Package’ that included assays for NS1, IgM, IgG and automated platelet enumeration. Blood samples were collected by venipuncture in the hospital laboratory. They were drawn into ethylene diamine tetraacetic acid (EDTA) coated tubes and tested for dengue components employing the single-step immunochromatographic *One-step dengue NS1 Ag and IgG/IgM test, Dengue Duo*, in accordance with the manufacturer’s instructions (Standard Diagnostics, Inc., St. Ingbert, Germany). The platelet enumeration was in the 5- or 3-differential analyzers, Coulter® T5diff AL (Beckman Coulter, Fullerton, CA, USA) or BC-3000™ (Mindary, Shenzhen, China). The individual reports were authenticated by two technologists and were available within 1–2 hours. Apart from the in-built controls in the *One-step dengue NS1 Ag and IgG/IgM test, Dengue Duo*, no independent controls from NS1 antigen, IgM and IgG were used. Data were entered and analysed using the Statistical Package for Social Sciences (SPSS Inc, Chicago, IL, USA, Version 11.5). Non-parametric testing was

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**Advances in Knowledge**

1. Concurrent assays for dengue virus non-structural protein 1 (NS1), anti-dengue IgM, anti-dengue IgG along with platelet enumeration in the ‘Dengue Package’ is immensely beneficial for patients, clinicians and public health officials.
2. Cases with a primary or secondary dengue virus infection in the initial febrile phase of illness will not escape detection with the ‘Dengue Package’.
3. Notifications to public health officials based on the results obtained by using the ‘Dengue Package’ would help in prompt initiation of anti-vector measures.

**APPLICATION TO PATIENT CARE**

1. The ‘Dengue Package’ produces an earlier differential diagnosis in suspected cases enabling appropriate intervention and prevention of any death from shock.
2. Patients with severe thrombocytopenia, when diagnosed as positive by use of the ‘Dengue Package’, can be offered platelet infusions immediately.
3. Clinicians can discontinue the empirical use of antibiotics in patients who test positive for dengue virus infection by use of the ‘Dengue Package’.
4. It should be possible to implement anti-vector measures around hospitalised patients found positive by use of the ‘Dengue Package’. Such measures will protect against any cross-infection on hospital premises.
Table 1: Platelet counts as 10^9/L in 678 cases screened NS1 positive by 'Dengue package' testing at Sant Parmanand Hospital during the 2010 dengue outbreak

<table>
<thead>
<tr>
<th>Category</th>
<th>Cases</th>
<th>Mean ± standard deviation</th>
<th>Standard error</th>
<th>Minimum platelet count</th>
<th>Maximum platelet count</th>
<th>Cases with counts &lt;20 x 10^9/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgM negative IgG negative</td>
<td>394</td>
<td>139.9±72.6</td>
<td>3.66</td>
<td>10</td>
<td>481</td>
<td>4</td>
</tr>
<tr>
<td>IgM positive IgG negative</td>
<td>145</td>
<td>100.0±52.9</td>
<td>4.39</td>
<td>11</td>
<td>274</td>
<td>1</td>
</tr>
<tr>
<td>IgM negative IgG positive</td>
<td>29</td>
<td>66.8±48.6</td>
<td>9.04</td>
<td>10</td>
<td>210</td>
<td>3</td>
</tr>
<tr>
<td>IgM positive IgG positive</td>
<td>110</td>
<td>69.6±45.1</td>
<td>4.3</td>
<td>10</td>
<td>206</td>
<td>12</td>
</tr>
</tbody>
</table>

Carried out. \( P < 0.05 \) was considered significant. The performance of this study was approved by the Director of our hospital.

Results

The patients tested by the "Dengue Package" were aged between 2 and 92 years, mean age 31.2 years: standard deviation (SD) 15.5 years, 95% confidence interval (CI) 2–62 years, 5th percentile 9 years and 95th percentile 62 years. In 678 patients, the NS1 antigen was detected with IgM and/or IgG while 1,208 were likewise NS1-negative. Among the 678 NS1-positive, 394 were exclusively positive for NS1, 145 were also positive for IgM, and 29 for IgG and 110 were positive for IgM and IgG (triple positive). The 1,208 NS1-negatives included 48 IgM-positives and 96 IgG-positives, while 122 were IgM-positive and IgG-positive and 942 were IgM and IgG negatives [Tables 1 and 2].

The platelet counts among the 678 NS1-positives were lower than the 1,208 NS1-negatives: the respective mean and SD were 116.8±70.2 x 10^9/L; 95% CI 167.2±94.0 x 10^9/L; 95% CI 90.7–98.2 [Figure 1]; the Mann-Whitney, 2-tailed test gave \( P = 0.002 \). The average platelet counts were highest among 394 who were exclusively positive for NS1, 140.0±72.6 x 10^9/L. They were lowest among 29 who were co-positive for IgG, 66.8±48.6 x 10^9/L; the Mann-Whitney, 2-tailed test \( P < 0.0001 \) [Figures 2 and 3]. There was no significant difference in platelet counts in cases who were positive for all three markers, 69.2±40 x 10^9/L, or those positive for NS1 and IgG and 66.8±48 x 10^9/L. The counts in 145 IgM co-positives, 100±52 x 10^9/L were higher than 110 triple-positives, 69.2±45 x 10^9/L; the Mann-Whitney, 2-tailed test gave \( P < 0.0001 \).

Among 1,208 NS1-negative cases, the average platelet counts were highest among 942 triple-negatives, mean 84.7±90.25 x 10^9/L and lowest among 122 positives for IgM and IgG, mean 86.1±77.7 x 10^9/L; the Mann-Whitney 2-tailed test gave \( P < 0.0001 \). The counts among 48 positive for IgM, 136.5±63.5 x 10^9/L were higher than for the 96 co-positives for IgG and IgM, 114.3±84.7 x 10^9/L; the Mann-Whitney 2-tailed test \( P = 0.028 \) [Figure 3].

Discussion

We initiated this feasibility study in August 2010 to ascertain the utility of concurrent testing of dengue virus NS1, IgM, IgG and platelet enumeration. The response was encouraging. Initial data on 175 suspected cases of dengue showed that just a single laboratory visit was sufficient both for serology and platelet enumeration; Consequently, the ‘Dengue Package’ was chosen by clinicians for patients with
febrile illness.

While working with the One step dengue NS1 Ag and IgG/IgM test, Dengue Duo, the in-built controls were used. For enumeration of platelets using different analysers, both internal quality control and external quality assessment were implemented. The performance of the BC-3000Plus (Mindary, Shenzhen, China) matched the results obtained on Coulter® TTm 5diff Autoloader (Beckman Coulter, Fullerton, CA, USA). The laboratory has participated in the Randox International Quality Assessment (RIQAS) programme for biochemistry for over three years; consequently, laboratory technologists are well trained in constant quality control.

The platelet counts among the 678 NS1-positives were lower than the 1,208 NS1-negatives: the respective mean and SD were 116.8±70.2 x 10^9/L, 95% CI 66.6–74.1 and 167.2±94.0 x 10^9/L, 95% CI 90.7–98.2 [Figure 1]; Mann Whitney, 2-tailed test gave P = 0.002. On average, the counts in exclusive NS1-positive cases were the highest, and lowest in those who were also IgG positives: 139.8±3.6 x10^9/L and 66.8±9.04 x 10^9/L. There was no significant difference in the counts in cases that were positive for all three markers and those positive for NS1 and IgG: 69.2±4 x 10^9/L and 66.8±9 x 10^9/L.

Among 1,208 NS1-negative cases, the average platelet counts were highest among those who were negative for IgG and IgM: 184.7±90.3 x 10^9/L and lowest among 122 positives for IgM and IgG: 136.5±63.5 x 10^9/L. Mann-Whitney, 2-tailed test gave P = 0.0001. The counts among 48 positives for IgM 114.3±84.7 x 10^9/L, 95% CI 90.7–98.2 were higher than the 96 co-positives for IgG and IgM, Mann-Whitney, 2-tailed, P = 0.0228 [Figure 3].

Among the 678 NS1-positive patients there were 394 who were negative for IgM [Table 1] and these would have otherwise been missed. They were suffering from a primary infection in the early phase of illness and were also viremic, i.e. they could transmit the virus if bitten by a mosquito. The 29 patients who were exclusively IgG positives, with a secondary viral infection, would have also been overlooked. Without NS1 screening they would have been labelled as “dengue negative”. They could have been infectious for mosquitoes during the earlier phase of illness. The concurrent NS1-positive and IgM-positive status of 145 patients [Table 1] reinforced the utility of antigen detection during the earlier phase of illness. Furthermore, 110 patients who were positive for NS1, IgM and IgG (triple-positives) [Table 1] were in the late stage of either a primary or a secondary infection and might have been infectious for mosquitoes. The NS1 test in the ‘Dengue Package’ helped in diagnosing an additional 423 (394 NS1 and 35 IgG positives) otherwise IgM negative cases. Those would have been labelled negative if the dengue IgM alone had been used. The NS1 negatives included 48 IgM positives who might have presented themselves for ‘Dengue Package’ fairly early during a secondary infection. A cell culture or reverse transcription polymerase chain reaction (RT-PCR) would be required to
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Exclusion of Dengue Virus Replication. Furthermore, 122 cases were positive for IgM and IgG [Table 2]. Such patients with a primary or secondary infection had presented in a later stage of illness. Dengue viruses are generally extruded from the host when IgM antibodies are present.

Among the 1,208 cases who were NS1-negative there were 942 triple-negative cases. It would not be possible to rule out dengue infection in the negative cases without testing for viral replication in cell culture and/or molecular investigations or immunofluorescence, or immunohistochemistry;1 facilities for these are not available in our hospital. Such patients should be investigated for acute febrile illnesses including malaria, urinary tract infection, enteric fever, Chikungunya virus and the influenza virus H1N1 infection.

Thrombocytopenia is observable in several patients with dengue virus infection. Cases with severe thrombocytopenia, platelet counts ≤30 x 10⁹/L (normal range = platelet counts of 150 to 400 x 10⁹/L), would need hospitalisation and/or platelet infusions.4 With the ‘Dengue Package’, it was possible to recognise 19 cases, four NS1 and IgM positive and three IgG positives [Table 1], and 12 triple-negatives [Table 2]. They would have missed detection during any one-tier combined screening for NS1, IgG and IgM.

Platelet counts were generally higher in NS1-positives than the NS1-negatives [Figure 1]. The average platelet counts in triple-negatives were highest. The counts were lowest among those with a secondary infection who were positive for NS1 and IgG [Figure 2]. In both NS1 positive and negatives, they declined further upon production of IgM and IgG antibodies. There was a progressive decline in counts in cases presenting in later stages of illness. The platelet count in 12 NS1, IgM and IgG-negatives was ≤20 x 10⁹/L. It would not be possible to rule out dengue infection in such cases without testing for viral replication in cell culture and/or molecular investigations or immunofluorescence, or immunohistochemistry.1 This would help to differentiate between patients with dengue-associated thrombocytopenia and those with severe bleeding episodes associated with trauma, invasive intensive care procedures or emergency surgery. Moreover, in patients with platelet count ≤20 x 10⁹/L, investigation for decreased megakaryocytic production, splenic sequestration, non-immune or immune destruction of platelets would need to be carried out.

The wide variation in the platelet counts of the patients [Tables 1 and 2] is natural since the mechanism of dengue related thrombocytopenia and coagulopathy is complex. It would involve platelet activation, pro-coagulant and anticoagulant arms of the coagulation system, complement, cytokines, and endothelial cells.7 Moreover, symptomatic thrombocytopenia would require platelet transfusion though platelet counts might not correlate well with clinical bleeding.

Public health officials were not notified about the 394 NS1-positive cases that were viremic and infectious to mosquitoes. Notifications are based on clinical and laboratory categorisation of a probable or confirmed case. As a rule rather than exception, WHO guidelines are applicable in dengue-endemic countries, including India.8 Nevertheless, IgM and/or IgG positive patients were notified as probable cases. A mandate for NS1-based notification is awaited. That would be ideal for future comprehensive reporting of every probable case of dengue.

The ‘Dengue Package’ was beneficial during the outbreak since a single laboratory visit for serology and platelet enumeration was an asset for clinicians and patients. Based on results obtained with the ‘Dengue Package’, platelet transfusion could be started straightaway. Those who were exclusively NS1-positives could be offered appropriate supportive therapy, thus avoiding any irrational usage of antibiotics. The patients and their attendants could be briefed regarding the basics of vector biology and provided with mosquito nets during hospitalisation.11 Moreover, with concurrent

Figure 3: Platelet counts as 10⁹/L in NS1-negatives as tested by the ‘Dengue Package’ at Sant Parmanand Hospital, Delhi.

Legend: 1 = Triple negative; 2 = IgG positive; 3 = IgG and IgM positive; 4 = IgM positive.
NS1 testing in the 'Dengue Package', one could even distinguish between a secondary or past infection in a patient positive only for IgG antibody; the demonstrable NS1 will indicate a secondary infection.

There were limitations in the present study, conducted during an outbreak of dengue with a three-fold higher than normal workload. There was no gold standard obtainable for authentication. Apart from the in-built controls in the One-step Dengue NS1 Ag and IgG/IgM test, Dengue Duo, no independent third-party controls were employed during the outbreak. Facilities for molecular testing or cell culture were not available. Some of the NS1-negative, but IgG and IgM positive cases, might have evolved from a NS1-positive status to a NS1-negative stage when examined by the 'Dengue Package'. Alternatively, there might have been other patients who had previously suffered from dengue virus infection. Unfortunately, none of them was available later to evaluate any seroconversion. Furthermore, precise details about the duration of fever and allied clinical presentations were not made available prior to the individual’s 'Dengue Package' testing in the hospital.

The 'Dengue Package' has substantiated the earlier utility of enhanced diagnostic sensitivity of the combined antigen-antibody testing protocols. To our knowledge, there are no reports that contradict the simultaneous use of the dengue NS1 antigen and antibody testing for disease diagnosis.

A combined antibody and NS1 diagnostic protocol was reported during the 2007 dengue outbreak in Puerto Rico. Employing a 90% plaque-reduction neutralisation test with dengue virus IgG depletion and NS1 antigen ELISA, it was possible to diagnose 85% of the 43 samples which could not be diagnosed using the standard diagnostic methods. During the multi-country evaluation of two commercially available NS1 ELISA assays, a combination of NS1 and IgM detection in samples during the first few days was recommended to increase the overall dengue diagnostic sensitivity.

Conclusion

Utilisation of the 'Dengue Package' can be important in the diagnosis of dengue virus infection in health care centres lacking sophisticated laboratory facilities as it means that one laboratory session would rule out dengue virus infection and also identify cases with severe thrombocytopenia who might have otherwise escaped detection. The 'Dengue Package' would enable physicians to offer rational therapy to their patients. They could
ask appropriate government agencies to initiate vector control measures including active disease surveillance. Last but not least, the one-stage 'Dengue Package' should emerge as the ideal option for the management of patients with dengue since it would be economical during dengue outbreaks even at secondary or tertiary care health centres. Dengue outbreaks overpower outpatient and inpatient facilities in hospitals and both medical and health care personnel are rapidly exhausted.

CONFLICT OF INTEREST
The authors reported no conflict of interest.

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References
Medical Tourism Abroad
A new challenge to Oman’s health system - Al Dakhilya region experience

Saleh S. Al-Hinai, Ahmed S. Al-Busaidi, Ibrahim H. Al-Busaidi

ABSTRACT: Objectives: This study aimed to understand why people seek medical advice abroad given the trouble and expense this entails. The types of medical problems for which treatment abroad was sought, preferred destinations and satisfaction with the treatment were explored. A secondary aim was to give feedback to stakeholders in the health care system on how to handle this issue and meet the needs of the community. Methods: 45 patients who had recently travelled abroad for treatment were asked to complete a questionnaire or were interviewed by telephone. Results: 40 questionnaires were received. 68% of the respondents were male. Orthopaedic diseases were the most common conditions leading patients to seek treatment abroad. Thailand was the most popular destination followed by India (50% and 30% respectively). 85% of respondents went abroad for treatment only, 15% of the patients experienced complications after their treatment abroad. Conclusion: Various facts about medical treatment abroad need to be disseminated to the public. This will necessitate greater effort in public health promotion and education.

Keywords: Oman; Medical tourism; Health care system.

Advances in Knowledge
1. Medical tourism abroad is a growing phenomenon that needs to be addressed carefully by health care authorities in Oman.
2. Public misconceptions about the standards of treatment abroad need to be addressed by extensive health education.

Applications to Patient Care
1. Patients interested in going abroad for medical treatment need to be handled prudently by their treating clinician.
2. Patients who insist on going abroad need to be appropriately guided and provided with all the relevant clinical data and evidence based medical information.

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In a globalising world, health care is no longer confined within national borders. Medical tourism is a new term used to describe the practice of seeking medical care abroad for non-emergency conditions. There is not yet an agreed international term for a person who travels abroad to seek medical treatment. Some experts label such patients “health tourists” or “medical tourists”. However, these terms suggest that travel abroad is for pleasure, which is at odds with the anxiety and pain often involved in seeking medical treatment. Therefore some prefer to refer to “medical travellers” even though the person might decide to combine his/her medical treatment abroad with tourism.

Globalisation has prompted countries to evaluate their position on trade in health services. The full extent of this trend is yet unknown, as data are sparse and anecdotal due to the absence of an internationally agreed definition and of a common methodology for data collection. This means that the limited statistics on medical tourism are often not comparable across countries; however, the available observations suggest that a substantial number of patients do travel to other countries for health care. For example, it is reported that Malaysia received 360,000 foreign patients from the Association of Southeast Asian Nations (ASEAN) region in 2007. According to a study by the World Health Organization’s (WHO) Regional Office for the Eastern Mediterranean, each year Jordan treats more than 120,000 non-Jordanian patients, generating an estimated US$ 1 billion in annual revenue. Regarding the number of residents from the USA travelling abroad for health services, a study by Deloitte Consulting estimated that 750,000 Americans travelled abroad for health services in 2007 and that this number would increase to 1.6 million by 2012. A study by the consulting firm, McKinsey, estimated that the number of US residents travelling abroad for medical care was estimated to range between 5,000 and 750,000 depending on the definition of medical travel.

In Oman, there is a national committee for treatment abroad which decides on the eligibility of candidate patients. The number of people it sent for treatment abroad was only 20 per 100,000 of the population in 2010 (so approximately 610 persons), down from about 59 per 100,000 in 1977 (information provided in email by the MOH’s Department of Treatment Abroad). The decline in numbers reflects the diminishing importance of treatment abroad following the development of health services in Oman. The total expenditure on treatment abroad by the Ministry of Health (MOH) in Oman in 2003 was US$ 2,563,171. Patients are sent to the UK (London), India and Germany. It was out of the scope of this study to measure the magnitude of medical tourism in Oman or even in Dakhilya region due to unavailability of statistics.

If this trend continues, experts are convinced that it will have major implications for public health systems around the globe. Despite the growing importance of medical travel, we still have little empirical evidence about its impact on public health, especially on health systems. The medical community in developed countries has started to recognise medical tourism as a real phenomenon that impacts the profession, practitioners and patients. Peer-reviewed medical and health journals began publishing papers on this topic in 2006. The medical tourism marketplace consists of a growing number of countries competing for patients by offering a wide variety of medical, surgical, and dental services. Some of the medical tourism companies hook patients up with a hospital and surgeon, arrange for their family doctors to send records and consult with the surgeons overseas, make travel arrangements and book hospital admissions.

They are many motivators for seeking treatment abroad such as: 1) Increased access to information about foreign health providers through the new developments in information technology; 2) Lower international transportation costs; 3) Reduced language barriers due to globalisation; 4) Treatments unavailable in the home country for legal, cultural or other reasons such as injections of stem cells; 5) Long waiting lists for certain procedures (UK and Canada), and 6) Inappropriate health insurance coverage (USA). However, researchers also found some barriers to medical tourism like the financial cost, fear of the unfamiliar and lack of confidence in foreign health care systems, discouragement by family doctors or treating physicians, and feeling too ill to travel.

Customers of medical tourism companies can purchase anything from cosmetic procedures and diagnostic examinations to kidney transplants, in vitro fertilisation, cancer therapies, and orthopaedic procedures. The cost of medical tourism packages
varies greatly. The prices depend on the types of procedures, where patients travel, how long they intend to stay, and whether they choose postoperative accommodation in budget hotels or luxury resorts.15

Medical travel has also raised several ethical issues. This is more evident when there are differential health policies in a particular country, i.e. one for the citizens as a public service and another standard for foreigners coming in as paying clients. Informed consent is a key ethical and legal issue as medical tourism companies are obliged to explain to patients the risks and benefits of medical procedures abroad.8 The potential exacerbation of health inequities in destination and source countries and the disruption of continuity of care for patients are other ethical concerns. The International Conference on Ethical Issues in Medical Tourism (ICEMT) raised three key points: 1) Medical tourism has the potential for cross- or inter-disciplinary research; 2) Medical tourism research must engage with empirical research from a variety of disciplines, and 3) Ethical analyses of medical tourism must incorporate both individual and population-level perspectives.16

Many countries, especially in the Far East, invest in this emerging industry in order to build a modern medical infrastructure that will attract foreigners and will create a new source of income while improving the medical services provided to the local community.21 To respond to the growth in medical travel, many countries have set guidelines and accreditation tools to regulate its quality. Examples are the Joint Commission (formerly the Joint Commission on Accreditation of Health Care Organizations) which initiated the Joint Commission International (JCI) to accredit hospitals worldwide,18 and the standards framework for regulating the medical tourism industry and Statement on Medical and Surgical Tourism.19,20 These tools address a number of concerns about this new industry and some of the safety and quality issues that patients may encounter if they seek health care services abroad.

The objectives of this study are thus threefold: first, to provide an overview of the main reasons and trends of patients travelling across borders from the Dakhilya region of Oman and their preferred destinations; second, to analyse the satisfaction rating of local treatment compared with that received abroad. Third, it aims to present the main challenges and areas for improvement for the health system and public health stakeholders in Oman as regards medical tourism.

Methods

The study was conducted in Al Dakhiliya region (in north central Oman) between March 2009 and August 2010. A questionnaire about medical tourism was developed after a literature review and discussion with colleagues in the Directorate General of Health Services, Dakhilya Region.

The questionnaire was composed of two sections. Section one collected demographic and other data (including age, sex, place of residence, date of diagnosis in Oman, date of treatment abroad and the country where treatment abroad took place). Section two had questions on the reasons for treatment abroad, its costs, quality and the outcome of the treatment and finally which part of the body needed treatment. The questionnaire was distributed to all those who travelled abroad for health care during above period. The subjects, who were mainly employees and all from the Dakhilya region, were enrolled in the study when they came to the Department of Health Affairs in the Directorate General of Health Services in Nizwa for countersignature of their sick leave permission from their places of work in order to travel abroad for treatment. Verbal consent was taken from participants for participation in the study and they were assured that refusal would not lead to any adverse consequences. Most of the subjects were given the questionnaire for completion. A few were interviewed by telephone when the person who came to obtain the sick leave countersignature was not the patient. The Omani National Treatment Abroad Committee pays the expenses of treatment of those patients sent by the government. Those going by themselves are not reimbursed. Those who were sent abroad for treatment by the government were excluded from this study because it was not their decision to travel abroad for treatment, therefore their answers as to reasons for travel, destinations and satisfaction would be biased. The data were analysed using the Statistical Package for the Social Sciences (SPSS, Chicago, IL, USA, Version 16). The chi square statistical test was used and the P value set at < 0.05. The study protocol
A new challenge to Oman’s health system - the Al Dakhilya region experience

Results

Out of 45 forms distributed, 40 forms were completed, returned and analysed (response rate 89%). All were completed by Omanis. Using descriptive analysis, the mean age of the study population was 38 years. The highest percentage of respondents was in the age group 31–40 years (31%). More males went abroad for treatment (67.5%) than females (32.5%). A total of 50% of the participants went to Thailand for treatment followed by India (30.0%), Iran (10.0%), Bahrain (7.5%) and United Arab Emirates (UAE) 2.5%. As to the distribution of clients according to their reason of travel, 85% of the participants travelled abroad to get treatment only; 10% for both treatment and tourism; 2.5% for a check-up, and another 2.5% for other reasons. About 85% of the study sample was treated in Oman before going abroad for treatment; thus, 15% went straight abroad for treatment without seeking treatment locally. The results of treatment of those treated inside Oman first are shown in Figure 1a. A total of 38.2% of the participants did not receive a specific diagnosis in Oman, and also 38.2% of the participants received treatment, but they did not find it beneficial.

More than 70% of the participants in the study got information about health institutions abroad from their friends and 18.9% from their family [Figure 1b]. The highest percentage of respondents went abroad for treatment for orthopaedic diseases followed by neurological and then ophthalmological disease [Table 1]. Using univariate analysis, those people aged 30–40 years had the most orthopaedic diseases (41.7%) followed by those aged 41–50 years (33.3%). Neurological diseases were also more prevalent in both age groups 31-40 and 41-50 years old compared to other age groups. Eye diseases were apparently more prevalent among people over 50 years old; however, due to the small sample size, the association between age and type of diseases ($P = 0.494$) was not statistically significant.

Male subjects went for treatment abroad mainly for orthopaedic diseases (28%), neurological diseases (28%) and gastroenterological diseases (24%). Females went for treatment abroad for orthopaedic diseases (38.5%), eye diseases (38.5%) and neurological diseases (15.4%). The association between type of disease and sex ($P = 0.116$) was, however, not statistically significant.

About one third of the participants stayed abroad for one week for treatment while 25% of the participants stayed 1–2 weeks. Those participants who travelled for orthopaedic, gastroenterological and neurological diseases preferred going to Thailand while those participants who sought treatment for eye diseases preferred to go to Iran; participants who sought treatment for cardiac

Table 1: Distribution of subjects according to type of disease

<table>
<thead>
<tr>
<th>Type of disease</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthopaedic</td>
<td>31.6</td>
</tr>
<tr>
<td>Neurological</td>
<td>23.7</td>
</tr>
<tr>
<td>Ophthalmological</td>
<td>18.4</td>
</tr>
<tr>
<td>Gastroenterological</td>
<td>15.8</td>
</tr>
<tr>
<td>Cardiac</td>
<td>7.9</td>
</tr>
<tr>
<td>Physiotherapy treatment</td>
<td>2.6</td>
</tr>
</tbody>
</table>

was approved by the Medical Research and Ethics Committee of the Directorate General of Health Services, Al Dakhilya region.
diseases preferred to go to India. The association between type of diseases and country ($P = 0.051$) was, however, not statistically significant.

Concerning cost, more than 60% of the participants spent less than 2,000 Omani rials (c. US $5,200) for treatment abroad while 38% of the participants spent more than 2,000 Omani rials [Figure 2]. A total of 45% of the participants who went to Thailand spent more than 2,000 Omani rials and 41.7% of the participants who went to India also spent more than 2,000 Omani rials whereas 75% of the participants who went to Iran spent 1,000–1,500 Omani rials. The association between the cost of treatment and the country of treatment ($P = 0.249$) was, however, not statistically significant.

We found that the percentage of satisfaction about treatment abroad was 100% in all countries except India where it was 83.3% giving an overall satisfactory percentage of 95%. There was no association between satisfaction with treatment and country ($P = 0.296$). A total of 15% of the participants developed some complications related to the treatment. These complications include pain, allergy, swelling and high blood pressure. Half of the participants had follow-up in governmental health institutions after coming back from abroad with 55% of them getting better [Figure 3]. Visits to Bahrain produced the highest percentage of treatment complications (33.3%) followed by India (16.7%) and Thailand (15%). The association between treatment complications and country ($P = 0.685$) was, however, not statistically significant.

**Discussion**

The sample size of this study was relatively small due to the difficulty of enrolling in the study those who travelled abroad for treatment because of the unavailability of a database. Nevertheless it revealed some interesting findings. Men travelled more than women probably since they are able to travel alone, while women, following Islamic and traditional customs, usually need a male companion. The overall mean age was 38 years which means that people tend to seek medical care abroad while they are young.

Due to low medical care costs in south Asian countries, India and Thailand were the most popular destinations for treatment abroad. This is contrary to a study of Saudi patients who travelled abroad for renal transplantation where the majority of transplant tourists obtained their kidneys in Pakistan (49%) followed by the Philippines (28%), Egypt (11%), and the United States (3.2%).

Although the majority of patients went for treatment only, it is interesting that some of them (10%) went for tourism as well. The explanation could be explained that they initially decide to go for tourism and then decide to obtain a medical check-up at the same time. This decision could also be influenced by the long delays and waiting lists at home. A study on reproductive health tourism in the United Arab Emirates (UAE) found that another reason for travel is privacy; this is a concern in an environment where both infertility and *in vivo* fertilisation are still stigmatised.

One of the interesting findings in our study is that 15% of the participants did not even seek any medical care locally, but rather travelled abroad directly although their illness could have been
managed locally. The reasons for such trend was not clear from this study so further studies may be necessary in future in order to explore this issue specifically.

Although dissatisfaction with local treatment was thought to be a major reason for seeking treatment abroad, this study showed only 5.9% of the participants were dissatisfied with local treatment. Concerning their source of information on treatment abroad, the Internet, newspapers and medical tourism offices were the least used sources (2.7% each); these are all available in Oman, but their low usage would indicate that people still intend to use traditional methods (such as word of mouth) as their source of information.

Although one may think that medical care abroad is cheap, overall costs are high. One third of participants in this study paid more than 2,000 Omani rials (c. US $ 5,200) for their treatment. This may give an insight into how much people may be ready to spend on their health. A case report from Bahrain showed that the prescription of 19 drugs, many of equivocal benefit, at a monthly estimated cost of US $ 615 imposed a substantial economic burden on the patient and led to poor adherence due to the confusing drug regimen.23

While it is thought that treatment abroad does not lead to complications, this study revealed that 15% of the participants indeed suffered some complications. This percentage may also be an underestimation since people may prefer not to report problems so as not to be blamed for seeking medical care outside their country. In addition, some complications do not manifest immediately; however, the subjects in this study responded to the questionnaire within days or at a maximum 2 weeks after their return from treatment abroad. Alghamdi et al. in 2010 showed that the group of ‘transplant tourists’ had a significantly higher rate of acute rejection within the first year compared with those who underwent local transplantation (27.9% versus 9.9%, P = 0.005). Also, compared with local transplantation, transplant tourists had a higher rate of cytomegalovirus (CMV) infections (15.1% versus 5.6%, P = 0.05) and hepatitis C seroconversion (7.5% versus 0%, P = 0.02).21 In 2011, Al Khaja reported on a Bahran patient who experienced adverse effects due to the polypharmacy prescribed abroad; these included nausea, vomiting, gastric pain, flatulence, severe constipation, tiredness, palpitation, nervousness and dizziness which compromised the patient’s quality of life and resulted in poor medication compliance.23

The most popular specialty for which people sought medical care abroad in this study was orthopaedics. This could be explained by the chronic nature of such diseases, its high prevalence, especially among the elderly, and the scarcity of specialist clinics in each health institution or region of Oman.

The limitations of this study included scarcity of data and statistics on patients who travelled abroad for treatment; this resulted in a small sample size. A further limitation is the shortage of scientific literature about medical tourism in Arab and Arabian Gulf countries. Further studies in these various countries, individually or as multicentre studies, are required to obtain a clearer picture of the treatment abroad trend.

Conclusion

This study has shown that it is very difficult to obtain data on patients who travel abroad for treatment. This therefore necessitates the establishment of national registries and databases. Many facts regarding medical tourism should be made clear to the community (e.g. treatment abroad can have some complications, is costly and that consultation with a local doctor is necessary prior travel). Modern technological methods for accessing information sources should also be advocated (i.e. Internet). Health education about the treatment of chronic diseases should be intensified so that people can decide whether there is chance for their illness to get cured abroad or not.

Specifically, two different approaches can be used to respond to the issues which this study raises in Oman about medical treatment abroad: the public health sector approach and the community approach.

First, the Omani public health authorities (the MOH and its sister institutions) need to pay more attention to this trend by establishing a national database and registry of treatment abroad which should be regular audited. Second, Omani authorities, in conjunction with those in the destination countries, should 1) Set standards as a framework for regulating the medical tourism
industry and encourage other countries to do so; 2) Accredit medical tourism companies and then regularly review their accreditation; 3) Mandate medical tourism companies to contribute to funds to protect clients from financial losses and to compensate them in case of complications or medical errors. Scientific conferences and workshops organised with other Gulf Cooperation Council (GCC) countries should also be encouraged in order to empower researchers and scientists to understand this phenomenon in our immediate region.

As to the community approach, the aim would be to raise awareness through the various media among all age groups in the community about medical tourism and its implication for individuals, families, communities and countries. Since it was shown clearly by our study that data and statistics about medical tourists are limited and difficult to trace, people should be requested to report to their primary health care institution on their return for recording and follow-up. Patients planning on medical tourism should know that they need to consult their local doctors first, use modern technologies (e.g. the Internet for browsing destinations options and offers), and be aware that complications can occur in treatment abroad. This awareness raising and education would be better undertaken as a multidisciplinary effort by various ministries, agencies and non-governmental organisations (NGOs).

CONFLICT OF INTEREST

The authors reported no conflict of interest.

References

20. Unti JA. Medical and surgical tourism: The new


Prevalence and Impact of Dysmenorrhoea among Omani High School Students

Rahma Al-Kindi and Anbarin Al-Bulushi

Abstract: Objectives: The objectives of this study were to determine the prevalence of dysmenorrhoea in Omani high schoolgirls, its impact and the treatment used. Methods: A cross-sectional survey was carried out in May 2010 on 404 girls from two public high schools in the Muscat region. Data were collected by self-administered questionnaire including information on demographics, prevalence of dysmenorrhoea, severity, its impact, and the treatment used. Results: Overall, 94% (n = 380) of the participants had dysmenorrhoea. It was mild in 27% (n = 104), moderate in 41% (n = 155), and severe in 32% (n = 121). Dysmenorrhoea was the cause of limited sports activities in 81%, decreased class concentration in 75%, restricted homework in 59%, school absenteeism in 45%, limited social activities in 81%, decreased academic performance in 7% of the affected students. Only 3% (n = 10) consulted a physician; 21% (n = 80) self-medicated, and 55% (n = 210) took no action. The commonest drugs used were paracetamol (n = 60, 16%), ibuprofen (n = 29, 8%) and mefenemic acid (n = 12, 3%). There was no statistically significant correlation between dysmenorrhoea, demographics and menstrual characteristics. Conclusion: Dysmenorrhoea is a prevalent and yet undertreated menstrual disorder among Omani adolescent schoolgirls. The pain suffered can be severe and disabling. Doctors should therefore be prepared to discuss this more freely with schoolgirls. In addition, there is a need for education regarding dysmenorrhoea and treatment options to minimise the impact on school, sports, social and daily activities.

Keywords: Dysmenorrhoea; Painful menstruation; Prevalence; Impact; Adolescent girls; High school; Students; Oman.

Advances in knowledge
1. This study is the first in Arabian Gulf countries to explore the prevalence of dysmenorrhoea in adolescent girls in high school.
2. This study has shown both a high prevalence of dysmenorrhoea and its huge impact on schoolgirls both academically and socially. However, adolescent schoolgirls seem reluctant to seek medical help for this problem.
3. This study will improve awareness among health care providers and allow them to be more sensitive to issues related to the management of dysmenorrhoea.
Dysmenorrhoea, or painful menstruation, is defined as painful cramps that begin a few hours before the onset of bleeding and may persist for hours or days. Dysmenorrhoea may be either primary, when there is no identifiable cause, or secondary to organic pelvic diseases. Primary dysmenorrhoea occurs typically between 17 and 22 years of age while secondary dysmenorrhoea is more common in older women. Dysmenorrhoea is commonly associated with systemic symptoms like lower back pain, nausea, vomiting, diarrhoea, fatigue and headache. The cause of primary dysmenorrhoea has yet to be established. It has been attributed to uterine contractions with ischaemia and production of prostaglandin. Based on the patient’s history, it is important to differentiate between dysmenorrhoea and premenstrual syndrome (PMS). PMS starts before the menstrual cycle and stops shortly after menstrual flow begins. The symptoms associated with PMS are more likely to be abdominal bloating and breast heaviness rather than lower abdominal cramps.1

Dysmenorrhoea is a common gynaecological complaint among adolescents and young adults. The prevalence rates reported for dysmenorrhoea vary widely across studies due to the differences in measurement methods. Prevalence rates have been reported to be as high as 93%2 and as low as 16%.3 In the Middle East, the prevalence of dysmenorrhoea in Egypt has been estimated to be 75%.4

Many adolescents consider dysmenorrhoea to be a normal part of the menstrual cycle and thus fail to report their pain to their physicians. The consequences of untreated primary dysmenorrhoea range from school absenteeism5,6 to disruption of relationships with family and friends.6,7

The risk factors reported in the literature for dysmenorrhoea are: age <20, nulliparity, higher/upper socioeconomic status, heavy/menses, attempts to lose weight, physical activity, smoking, disruption of social networks, depression and anxiety;10 however, studies have been quite heterogeneous in terms of association.

Although dysmenorrhoea is an important public health problem, there has, to our knowledge, not been any data published from Oman. In order to lay the groundwork for such an undertaking, studies are needed to establish the prevalence of dysmenorrhoea in adolescent Omani girls. The bulk of the population in Oman is in the adolescent age group.11 Therefore, this study aims to quantify the prevalence of dysmenorrhoea in adolescent schoolgirls and its impact on school performance as well as the treatments used. An integral part of the present study is to ascertain the associated risk factors among adolescent schoolgirls with dysmenorrhoea.

Methods

A cross-sectional survey was carried out in two female public high schools, namely Al Hail Alawamir and Omama bint Alaas, in May 2010. The two schools were randomly selected out of four high schools in the Al Seeb area of the Muscat region. Like most of the high schools in the Muscat region, each school has around 1,500 students in 50 classes of grades 11 and 12, the students’ ages ranging from 15 to 23. In each school, 4 classes from each grade were randomly selected. A total of 16 classes were studied. The survey was conducted during school hours and included a total of 404 students.

A pre-tested and structured questionnaire was developed by the authors based on a pilot study and thorough review of relevant literature addressing...
the prevalence and severity of dysmenorrhoea, the impact of dysmenorrhoea on daily activities and the prevailing management strategies. The participants were briefed on the objectives of the study and the definition of dysmenorrhoea was explained as any lower abdominal pain or discomfort associated with the menstrual period. The degree of pain was categorised by a multidimensional scoring system as mild, moderate and severe based on pain, limitation of activities and medications taken. Mild pain was defined as “painful menstruation that seldom inhibits normal activity and analgesics are seldom required”; moderate pain as “painful menstruation that affects daily activities and analgesics are required and give relief”; severe pain as “painful menstruation that clearly inhibits daily activities and the pain is not totally relieved by analgesics.” The amount of bleeding was defined depending on the number of pads used per day as little (<4 pads per day), moderate (5–10 pads per day) and heavy (2 pads at a time). Information was gathered on the students’ age, grade, residency, and family history of dysmenorrhoea. Questions related to menstruation elucidated their age at menarche, regularity of the cycle, length and duration of the cycle, amount of bleeding (little, moderate or heavy), pain during menstruation, severity of the pain (mild, moderate or severe), associated symptoms, premenstrual symptoms, their impact on daily activities and absenteeism from school, and treatment taken, if any. The weight and height of the participants was measured by the researchers and/or trained research assistants. The cut-off points for body mass index (BMI) were based on recommendations by the World Health Organization’s (WHO) Expert Committee on Physical Status. Data was collected using a self-administered questionnaire. The researchers and/or research assistants were available on site to assist the students in completing the questionnaire which took 20 to 30 minutes. Students who had not yet experienced the menarche, or had gynaecological diseases, had had abdominal or pelvic surgery, or refused to give consent, were excluded from the analysis. The participation was therefore on a voluntarily basis with written consent being taken before initiating the data collection. Anonymity and confidentiality was assured and emphasised. Ethical approval for the study was granted by the Medical Research and Ethics Committee of Sultan Qaboos University, College of Medicine and Health Sciences in 2010. Permission to distribute the questionnaires in schools was obtained from the Directorate General of Muscat Region, Ministry of Education.

STATA software (StataCorp LP, Texas, USA, Version 10) was used for data entry and analysis. Frequencies and percentages were computed for discrete variables and the mean and standard deviation were computed for continuous variables. The Pearson’s χ² tests (or Fisher’s exact tests for cells less than 5) were used as appropriate to test the association between dysmenorrhoea and the studied variables. The 5% level of significance was taken to test the significance of the obtained results.

Results

This study included a total of 404 Omani students; 200 (49.5%) were from Al Hail Al Awamir School and 204 (50.5%) were from Omama bint Alaas School. Nearly two thirds of participants (n = 259, 64%) were in grade 12 and one third (n = 145, 36%) were in grade 11. Their ages ranged from 15 to 23 years, with a mean of 17.50 (±0.98) years. The vast majority of students were originally from the Muscat region (n = 344, 85%). Nearly half of the participants (n = 212, 52%) were of normal weight; 90 (22%) were underweight and 102 (25%) were overweight and/or obese. The age at menarche ranged from 9 to 17 years. The mean age at menarche was 13.00 (±1.31) years. The sociodemographic data and characteristics of the menstrual cycle are given in Table 1.

Regular cycles were reported by 59% (n = 237) of the students; a cycle duration of 21 to 35 days was reported by 89% (n = 359); menstrual duration of 2 to 7 days was reported by 88% (n = 354), and little to moderate flow was reported by 95% (n = 382). The overall prevalence of dysmenorrhoea was 94% (n = 380). Of the participants with dysmenorrhoea, the pain experienced was reported as mild by 27% (n = 104); moderate by 41% (n = 155), and severe by 32% (n = 121). There was no statistically significant correlation between dysmenorrhoea and the following: age at menarche, regularity of the cycle, length and duration of the cycle, reported amount of flow, BMI, and family history of dysmenorrhoea at (P >0.05) [Table 1].

All the participants with dysmenorrhoea
reported some associated symptoms. The most frequently reported symptoms were backache (n = 302, 79%), stomach cramps (n = 266, 70%) and mood changes (n = 260, 68%). Table 2 shows the most commonly reported symptoms associated with dysmenorrhoea. A total of 39% percent of the
participants (n = 147) suffered from some form of PMS, of which the majority reported backache (n = 103, 27%) and/or irritability (n = 90, 24%). The other symptoms reported were loss of appetite (n = 74, 19%), gastrointestinal symptoms (n = 68, 18%), abdominal bloating (n = 63, 17%), headache (n = 56, 15%), breast heaviness (n = 50, 13%) and skin changes (n = 19, 5%). Over two thirds of the participants (n = 276, 73%) had not sought treatment for their pain, with only 3% (n = 10) having consulted a physician. The majority of participants with dysmenorrhoea (n = 300, 79%) did not take any medications. Paracetamol (n = 60, 16%), ibuprofen (n = 29, 8%) and mefenamic acid (n = 12, 3%) were the most commonly used analgesics. Others reported using complementary and alternative medicine in the form of herbs (n = 47, 12%) and a heating pad (n = 45, 12%).

Almost all the participants with dysmenorrhoea (n = 377, 99%) reported that the pain adversely affected their daily activities. Among the participants, 308 (81%) limited their sports activities, 285 (75%) reported decreased concentration in the classroom, and 226 (59%) complained of a diminished ability to do homework. There were 170 (45%) students who endorsed the idea that dysmenorrhoea made them miss classes, 94 (25%) reported a limitation of social activities and 32 (8%) had experienced decreased academic performance.

Table 2: Percentage of participants with dysmenorrhoea who suffer from associated symptoms (more than one symptom per person)

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Participants with associated symptoms (n = 380)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td>Backache</td>
<td>302</td>
</tr>
<tr>
<td>Stomach cramps</td>
<td>266</td>
</tr>
<tr>
<td>Mood change</td>
<td>260</td>
</tr>
<tr>
<td>Myalgia</td>
<td>227</td>
</tr>
<tr>
<td>Fatigue</td>
<td>194</td>
</tr>
<tr>
<td>Nausea</td>
<td>157</td>
</tr>
<tr>
<td>Headache</td>
<td>139</td>
</tr>
<tr>
<td>Dizziness</td>
<td>100</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>92</td>
</tr>
<tr>
<td>Vomiting</td>
<td>61</td>
</tr>
<tr>
<td>Edema</td>
<td>19</td>
</tr>
</tbody>
</table>

Discussion

This study provides new information not previously available from Oman, or even from the neighbouring Arab/Islamic countries of the Gulf, on the prevalence, impact and treatment of dysmenorrhoea in adolescent high schoolgirls. This study found the prevalence of dysmenorrhoea in girls in high school to be 94% of the cohort surveyed. Estimates of the prevalence of dysmenorrhoea range between 16% and 93%. The rate of dysmenorrhoea revealed by the present study is comparable to the 90–93% reported from USA, Iran and Canada, but it is higher than the rates reported from Egypt, Nigeria, Turkey and India that ranged between 25–80%. The wide variation in these estimates may be attributed to the use of differently selected groups of subjects and the absence of a universally accepted definition of dysmenorrhoea and system for grading its severity. Another reason for the variation could be due to ethnic and sociocultural factors. Differences among ethnic groups have been reported in Western as well as Asian communities; however, it remained unclear whether the variation was related to biological or cultural factors.

Of this study population, 32% reported having severe dysmenorrhoea which is twice the prevalence reported in a similar study in Egypt. More than two third of the participants (73%) described their pain as moderate to severe. This indicates that although dysmenorrhoea may be a furtive illness, its prevalence is high and therefore has an implication on the quality of life and public health.

Some studies have shown a link between dysmenorrhoea and several risk factors including early menarche, irregular or long cycles and heavy menses. However, this study did not find any significant association between dysmenorrhoea and age at menarche, regularity of the cycle, length and duration of the cycle, amount of flow, BMI, or family history of dysmenorrhoea. This could be due to the small sample size, a very homogenous group and the fact that pain is experienced subjectively and therefore difficult to measure. It remained unclear if the high prevalence of dysmenorrhoea among Omani high schoolgirls in our study is related to biological or cultural factors, and further studies are needed to explore these issues.

Dysmenorrhoea is known to be associated with
a wide variety of physical symptoms. Backache and stomach cramps were the two most common reported symptoms in our study, and similar to findings elsewhere in the literature. On the other hand, PMS is also known to be associated with a wide variety of symptoms like abdominal bloating and breast heaviness. The distinction between the two may not have been clear to the participants thus leading to over-reporting of dysmenorrhoea.

The results clearly showed that dysmenorrhoea adversely affected the students’ daily activities. Dysmenorrhoea had an adverse effect on school performance reflected in low concentration during classes, difficulties in accomplishing homework and school absenteeism. It also limited participation in sports and social activities. This is consistent across different cultures, supporting an underlying biological origin of dysmenorrhoea.

Despite the considerable impact of dysmenorrhoea, both academically and socially, only 3% of the participants with dysmenorrhoea had consulted a doctor about it. This is consistent with other findings that most adolescents with dysmenorrhoea do not consult a health care provider. We found that 21% (n = 80) of the participants self-medicated by drugs like paracetamol, ibuprofen and mefenemic acid. The low rates of self-treatment and physician consultation rates may be due to the sensitive nature of dysmenorrhoea among adolescent girls, conservative social values and cultural beliefs, and the reluctance of young unmarried girls to consult a physician, particularly a male physician. We also found that more than half of the participants did nothing to alleviate their pain. Likewise, studies in Egypt, Nigeria, Turkey and India reported that more than half of the adolescents studied did not seek treatment for dysmenorrhoea. This may suggest that there is a significant lack of awareness and knowledge among adolescent girls regarding treatment for dysmenorrhoea. Our study did not investigate barriers to seeking medical attention for dysmenorrhoea; nevertheless, the participants’ responses indicated that many girls accept dysmenorrhoea as a normal aspect of the menstrual cycle and believe that it cannot be treated. These ideas likely provided the rationale for not seeking medical treatment. Improving the girls’ knowledge about dysmenorrhoea could therefore positively influence their healthcare-seeking behaviour. Health promotion in the primary health care setting or at school may be an efficient way of achieving this.

There are several limitations to the current study. Although girls with potential causes of secondary dysmenorrhoea were excluded from the study sample, it was not possible to discriminate between primary and secondary dysmenorrhoea in this study population. In addition, despite the fact that the definition of dysmenorrhoea was explained before the questionnaires were completed, some of the responses may reflect general experience rather than specific menstrual discomfort. The self-reporting nature of this study may have resulted in recall bias and over-reporting of the condition. Besides, it is possible that some of the participants completed their questionnaires with peers, which may have biased their responses. Finally, this study was conducted in only two schools of Muscat region; the results may therefore not be generalisable to other regions or to the entire country.

**Conclusion**

This study unequivocally suggests a high prevalence of dysmenorrhoea among Omani girls in high school indicating that it is a significant health problem needing attention. Young girls are unlikely to discuss dysmenorrhoea with their family physician, or seek painkillers available over the counter. They seem to accept dysmenorrhoea and its consequences as part of the physiological process of the transition between adolescence and adulthood. This reflects a shortage of information about primary dysmenorrhoea targeted at female adolescents. Health education on issues related to reproductive health should be incorporated early enough in the school curriculum to prepare girls for menstruation and inform them about available treatment options in case they experience dysmenorrhoea. A number of professionals can play a crucial role in educating young people especially family physicians and school personnel.

**CONFLICT OF INTEREST**

The authors reported no conflict of interest.

**ACKNOWLEDGMENTS**

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References

السيطرة على المعلومات، الرعاية الصحية الفعالة، الممارسة المبنية على الدليل وجرّاح الأنف والأذن والحنجرة

دبيا بيارجافا، يوسف السعدي، كامليش بيارجافا، راشد العبري

المتخصّصون الهدف: دراسة طريقة سلوك الحصول على المعلومات لدى جرّاحي الأنف والأذن والحنجرة في عمان، وربطنه بالتعلم واستكمال مهارات الممارسة المبنية على الدليل. الطرق: أجريت هذه الدراسة المقطعيّة عبر توزيع استبيان على 63 من الجراحين العاميين ممارسين لجراحة الأنف والحنجرة في عمان (تشمل مختلف جزيئات التخصص من التخصص إلى الاستشاري) أثناء حضورهم مؤتمراً وطنياً لجراحة الأنف والأذن والحنجرة في يناير 2010. النتائج: تم استخدام تسعة وأربعين استبيانًا كامليلاً. وكان لدى 57% من المشاركين خبرة تزيد عن 10 سنوات، وكان 60% منهم يعملون في مستشفى الرعاية التلقائية. ظهر أنّ 38.8% منهم على الافق تام و 36.7% على الافق جزئي. بأن الممارسة المبنية على الدليل من شأنها تحسين نوعية الرعاية، وبالتالي تقدم رعاية صحية عالية الجودة. كان لدى أكثر من 18.4% من المشاركين تقبل مثالي للإدارة والمتابعة (11% - 38.8%) من المشاركين تقبل مثالي للإدارة والمتابعة. 46.9% من الجراحين استعداداً للاكتساب مهارات السيطرة على المعلومات. كانت هناك علاقة إيجابية بين عدد سنوات الخبرة، وعدد الأسئلة والرغبة في اكتساب مهارات السيطرة على المعلومات. الخلاصة: تبنت ارشاد أدهم صحرار الشبكة الدولية لأداء الممارسة السريريّة. ملاحظة: معظم الجراحين العاملين في جراحة الأنف والحنجرة في عمان لا يقبلون أن يكون بعضهم يفتقد من اكتساب مهارات المعلومات فحسب. بل إن الرعاية الصحية الفعالة تعتمد على هذه المهارات وعلى الممارسة المبنية على الدليل. وأظهرت هذه الدراسات أن اكتساب استخدام هذه المهارات سيكون حيويًا في المستقبل لمساعدة الجراحين بهذا الاتجاه. قلّة في الرعاية الصحية الفعالة.

مفتاح الكلمات: إدارة المعلومات، رعاية صحية فعالة، عمان، طب مبني على الدليل، ممارسة مبنية على الدليل، الشبكة الدولية.

ABSTRACT: Objectives: The objectives of this study were to study the information-seeking behaviour of otolaryngologists in Oman, and their willingness to learn and acquire evidence-based practice (EBP) skills.

Methods: A cross-sectional survey was carried out by distribution of a questionnaire to 63 otolaryngologists (ranging from residents to consultants) employed in Oman who attended a national otolaryngology meeting in January 2010.

Results: Forty-nine completed questionnaires were received; 57% of the respondents had more than 10 years’ experience, and 60% were from tertiary care; 38.8% “totally agreed” and 36.7% “partially agreed” that EBP would improve the quality of care and thus provide effective health care to patients. More than 46.9% had 1–5 questions per week, 18.4% had 11 or more questions per week at the point-of-care; 69.4% were willing to acquire information mastery skills. There was a statistical correlation between the number of years of experience, the number of questions, and willingness to acquire information mastery skills.

Conclusion: In today-to-day clinical practice, web-based resources are of increasing significance. Most otolaryngologists in Oman not only believed that it is essential to acquire information mastery skills, but also that effective health care depends on such skills and on EBP. Most were willing to acquire these skills. In these fields, these skills will be vital in helping otolaryngologists deliver effective health care solutions.

Keywords: Information Management; Effective health care; Oman; Evidence-based medicine; Evidence-based practice; Internet; Point-of-care.
The goal of medicine has always been to provide care to patients in a way that will help them live to their fullest capacity with the minimum amount of pain and discomfort. Not only has the identification of ways to provide better medical care improved, but also this information is coming to us at an accelerated pace. New treatments are constantly being found, and older approaches are continually becoming obsolete. Physicians and surgeons are being asked to retool their whole approach to information. Now they have to be information managers, continually learning and updating their approach to medical care as medical knowledge continues to evolve.

Information mastery has been defined as “applied science that allows clinicians to harness resources in the information age.” It is a set of skills that will help medical professionals be as up-to-date as their patients by obtaining the most valid and relevant information in the least amount of time.1

Information mastery was defined as: Usefulness of an information = Relevance x Validity

Work

The usefulness of any information is directly proportional to its relevance and its validity; however, if too much work is required to obtain that information its usefulness diminishes.1 Information mastery is an outgrowth of the movement towards evidence-based medicine (EBM), which first started in 1981.2

The constant increase in the body of medical knowledge is a source of frustration and anxiety amongst health professionals in general and medical students in particular. Every day new diagnostic tests and treatments are being introduced. Patients are also becoming better informed through the media and the Internet stimulating a new passion for life-long learning in academia, professional environments, work place and at home.3 There is a need for evidence-based knowledge at the point-of-care as most physicians and surgeons have unmet information needs, besides day-to-day clinical dilemmas and differences in opinions. Medical research continues to expand at an exponential rate. The task of clinicians striving to practice EBM medicine seems to be getting bigger with doctors increasingly having to rely on Internet-based resources.4

Today otolaryngologists are not expected to know everything, but should be able to access and assess information when required, to be information masters rather than encyclopedias of medical information. The aim of this study is therefore to examine the information-seeking behaviour and attitudes to information mastery and EBM.

Methods

This cross-sectional study was carried out in January 2010 at the annual meeting of otolaryngologists in Oman. All sixty-three otolaryngologists present were requested to participate in the study by completing a questionnaire which was distributed to them.

The questionnaire was created and designed by two co-authors of this article (DB and KB). It comprised 4 sections and 15 statements/questions. Questions covered demographics (including number of years of experience); information mastery needs; availability of information mastery tools, and attitudes to information mastery and EBM.

The questionnaire was subjected to internal and external validation. Internal validation included evidence-based practice (EBP) in day-to-day practice.

3. The knowledge that 69% would like to acquire skills for practising EBP would help in determining the educational needs of this cohort.

4. The study revealed a direct statistical correlation between otolaryngologists with less than 5 years clinical experience and a reluctance to acquire EBP skills; this cohort also had fewer questions arising from their day-to-day practice of otorlaryngology. This needs to be addressed if effective health care is to be provided to patients in Oman by future otolaryngologists.

Applications to Patient Care

1. This study showed that otolaryngologists, faced by information overload, lack of time, assessments of quality of care and patients informed by internet research, can improve their knowledge, the quality of their care, and protect themselves from litigation by acquiring information mastery skills.

2. Information mastery skills can help in solving day-to-day clinical dilemmas and differences of opinion, and meet currently unmet information needs at the point of patient care.
piloting the questionnaire with four experts who analysed its linguistic, face, and content validity. Following internal validation, the questionnaire was edited and arranged in a logical, brief, simple, clear, concise, unambiguous and user-friendly format; unnecessary and repetitive questions were detected and deleted. The effectiveness of the questionnaire was determined by the survey itself and its reliability was found to be satisfactory.

The data were analysed using the Statistical Package for the Social Sciences (SPSS, Chicago, IL, USA, Version 16) and correlations were studied. The significant differences in the percentages between the groups were studied using the chi-square test. A P value (two tailed) of less than 0.05 was considered statistically significant.

Results

A total of 49 completed questionnaires were received. The demographic data is shown in Table 1. A total of 57% of respondents had more than 10 years experience, while 60% were from tertiary care. A total of 38.8% “totally agreed” and 36.7% “partially agreed” that EBP would improve the quality of care [Figure 1].

“Questions” were defined as questions which required the otolaryngologists to undertake further investigations during the care of a specific patient. More than 46.9% had 1–5 questions per week at the point-of-care; 18.4% had 11 or more questions per week. A significant finding was that 12% had less than one question per week; all these responders had less than 5 years of experience [Figure 2].

On the topic of information mastery skills, 69.4% of respondents were willing to acquire them. There was a statistical correlation between the number of years of experience, the number of questions, and willingness to acquire information mastery skills. These results reveal that more experienced otolaryngologists had higher information needs, and vice versa [Figure 3].

Discussion

This study examined the impact of information technology, with a EBP focus, on the way otolaryngologists in Oman sought to answer clinical queries. Most of the otolaryngologists (75.5%) agreed partially or totally that the quality of health care depended on evidence at point-of-care and that EBP would improve the quality of care. It would have been interesting to know the thoughts of the respondents regarding factors other than EBP that influenced the quality of patient care, but that was outside the scope of the present study.

There was a positive correlation between the number of years of experience and the number of questions which occurred each week. This finding is in contradiction to the expectation that lesser-experienced surgeons would have more questions. Some of the possible explanations for the junior otolaryngologists’ small number of weekly questions and low interest in developing information mastery skills could be lack of time, other priorities, a preoccupation with developing surgical skills and the need to study for examinations. This attitude
needs to be addressed in the interest of the quality of their education and patient care with the ultimate goal of enhancing their skills in both knowledge-acquisition and surgery. In a study carried out in 1994, Covell et al. found that physicians had two questions for every three patients seen, and that 40% of clinical questions raised during in-patient consultations were on medical facts.6 These findings appear similar to those found in the present study where more than 46.9% of respondents had 1-5 questions per week. Translating knowledge into practice can close the gap between good and best care. No matter what source we choose, we would like to spend the least amount of time and energy to find the best information.7 The problem with using clinical experience alone is its validity although certainly using one’s own experience to meet information needs involves minimal work. A study conducted in the USA showed that 49% of causes of family physician errors, as perceived by physicians, were due to a lack of knowledge about the medical aspects of the case.8 In another study, it was also found that family physicians do not pursue answers to 64% of their clinical questions, but when answers are pursued, they can be found for 80% questions.9 We have a very similar experience in our team as invariably as we have been able to retrieve answers to most of the clinical questions asked. The imperative of training junior doctors to utilise information technology resources competently was found to be a strongly held belief among responders in a somewhat similar study of paediatricians;9 however, the provision of access to online resources may not result in the application of EBM to patient care. In a survey of UK paediatricians carried out while they were on call, Riodan et al. found that very few of them used EBM resources to make on call decisions although they had access them.10 They concluded that a better utilisation of resources might be to train doctors to be ‘practitioners of EBM’ and so to know where to find preprocessed evidence and how to apply it—rather than be able to perform complex critical appraisal through training in clinical epidemiology. In a review of online evidence-based resources, Krupski et al. commented that the use of electronic databases of pre-appraised evidence can greatly expedite the search for high quality evidence. This can then be integrated with the patient’s individual circumstances to provide translational research at the point-of-care.11

The study had some limitations: the small number of otolaryngologists in Oman, and a limited representation of them at the meeting where the data was gathered. Another limitation was that the survey respondents ranged from junior to senior otolaryngologists.

### Table 1: Demographic data on the survey respondents

<table>
<thead>
<tr>
<th>Demographic Category</th>
<th>Percentage of respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GRADE</strong></td>
<td></td>
</tr>
<tr>
<td>Consultants</td>
<td>37</td>
</tr>
<tr>
<td>Specialists</td>
<td>22</td>
</tr>
<tr>
<td>Postgraduate trainees</td>
<td>41</td>
</tr>
<tr>
<td><strong>AGE GROUP</strong></td>
<td></td>
</tr>
<tr>
<td>&gt;40 Years</td>
<td>57</td>
</tr>
<tr>
<td>&lt; 40 Years</td>
<td>43</td>
</tr>
<tr>
<td><strong>GENDER</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>47</td>
</tr>
<tr>
<td>Male</td>
<td>53</td>
</tr>
</tbody>
</table>

**Figure 3**: Relationship between number of years of experience and willingness to acquire information mastery skills for evidence-based practice (EBP).

**Conclusion**

In day-to-day clinical practice at the point-of-care, Internet resources are of increasing significance. In this study, most otolaryngologists believed that quality of care depended on EBP and information mastery skills. The number of clinical queries at the point-of-care was directly correlated to the number of years of clinical practice experience of the respondents. Most of the
otolaryngologists surveyed were willing to acquire information mastery skills. The reluctance of junior otolaryngologists to acquire these skills in addition to surgical skills needs to be addressed. To address the ever changing world of medical knowledge and to keep up with the advances in medicine, we propose that otolaryngologists should incorporate into their practice the skills of information mastery in order to keep updated, and provide the best possible care thus improving the quality of care and the patients’ health-related quality of life.

CONFLICT OF INTEREST
The authors reported no conflict of interest.

References
Laparoscopic Surgery Recording as an Adjunct to Conventional Modalities of Teaching Gross Anatomy

Pananghat A. Kumar, Mark Norrish, Thomas Heming

ABSTRACT: Objectives: In order to increase their effectiveness, methods of teaching morphological sciences need to be revised to incorporate the recent technological advances made in the field of medicine. Teaching human structure with conventional methods of prospection using dissected cadaveric specimen alone quite often fails to prepare students adequately for their clinical training. A learner-oriented method, incorporating three dimensional spatial anatomy and more closely mirroring the clinical setting, is required. Methods: With these challenges in mind, a 30-minute slow-paced video recording of a cholecystectomy performed laparoscopically on a 45 year-old lady was adapted to supplement the conventional teaching of anatomy of the abdomen and pelvis. This study was carried out in October 2010. Results: The subjects of this study were 84 students in a first year preclinical MD course in human structure at the private Oman Medical College. Their feedback was obtained via questionnaire and revealed that the video presentation helped the students to realise the significance of the anatomy required for a medical career and led to remarkable changes in the nature of anatomical knowledge required by a clinician. It has therefore become necessary to review teaching strategies to ensure that these newly desired learning outcomes are addressed. Although the curricula used in medical schools worldwide are diverse, the level of anatomical knowledge required to become an efficient clinician remains agreed upon. Until recently, the conventional method of learning the subject by dissection of human cadavers and didactic lectures has served its purpose. With the advent of modern surgical techniques and intervention devices, the nature of living anatomy required for a medical

Keywords: Laparoscopic surgery recordings; Video recording; Abdominal cavity; Medical education.

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RECENT TECHNOLOGICAL ADVANCES have revolutionised the realm of patient care and led to remarkable changes in the nature of anatomical knowledge required by a clinician. It has therefore become necessary to review teaching strategies to ensure that these newly desired learning outcomes are addressed. Although the curricula used in medical schools
student has changed immensely. There has also been a growing tendency to replace the hours of dissection with prospected specimens, anatomical models and simulated procedures as a result of the dearth of conventional learning resources including cadaveric material, and the reduction in time allotted to anatomy teaching. It has been suggested that this reduced attention to anatomy has resulted in a situation, in many medical schools, where undergraduate education in anatomy is below the minimum necessary for safe medical practice. This has led to calls for the 21st century curriculum to move from the passive, didactic and highly detailed courses that used to be taught towards more functionally and clinically relevant modes of teaching. The introduction of a laparoscopic video presentation into a preclinical anatomy course is one example of this trend.

Whatever the methods used to teach anatomy, it is very clear that the learner needs to comprehend the three-dimensional structure and the spatial relations of the organs in as live a manner as possible in order to apply this knowledge in later clinical practice. Radiological images and videos of laparoscopic procedures seem to be resources of choice to address this issue. Laparoscopic training using embalmed cadavers has been used in some schools of medicine, but it has mainly been centered on reviewing basic anatomy for clinical students and residents in specific specialities and principally designed to develop laparoscopic skills in surgical trainees. The main hindrance to this method has been the fact that the cadaveric material does not show the flexibility of tissue and the liveliness of the organs. To circumvent this problem, Thiel embalmed cadavers that maintain the colour, consistency and flexibility of a live body, and avoid rigor mortis changes, have been used to simulate minimally invasive techniques and to review the clinical trainees’ knowledge of anatomy. However, information regarding the structured use of laparoscopic surgery to teach preclinical students seems to be scanty. In an attempt to enhance the learning outcomes of preclinical students, it was decided to test the use of a video of a laparoscopic procedure to supplement the conventional methods employed in teaching anatomy of the abdomen and pelvis to preclinical students in a private medical school in Oman.

**Methods**

Eighty-four students took part in this study as part of their regular teaching programme: a mandatory course in human structure (anatomy) in their first preclinical year of medical studies. All of the students were enrolled in a full time degree in medicine (MD), after three years of premedical studies. The study was carried out during October 2010. It was part of ongoing research into improving teaching and learning in medical education and, as such, conformed to all of the ethical requirements and had the approval of the institutional review panel for ethics.

A video of a cholecystectomy performed laparoscopically on a 45 year-old lady was used to supplement the module on the anatomy of the abdomen and pelvis. The laparoscopic procedure had previously been explained to the patient and informed consent obtained to use the video for teaching medical students.

The video presentation, which lasted approximately thirty minutes, was preceded by a lecture introducing laparoscopic surgery and the steps involved in it. In the first part of the video, prior to the surgery and soon after establishing the pneumoperitoneum, the consultant surgeon scanned the abdomen of the patient with the camera to provide a ‘laparoscopic excursion’ of the abdominal cavity thereby demonstrating the general anatomy of the region and the disposition of the viscera in situ. The video showed the abdominal surface of the diaphragm and subsequently the anterior abdominal wall, the general outlay of the peritoneum and the disposition of the abdomino-pelvic organs. The video was presented at a slow pace, with frequent pauses and with a live commentary on the structures seen, allowing time for the students to observe and appreciate all the major structures within the abdominal cavity in situ. These included the greater omentum, the lesser omentum and the abdominal organs and also the major pelvic organs. Peristalsis of the intestines, the ureter and the pulsations of the mesenteric arteries were all clearly visible and well appreciated in the video. In the second part of the video, the gall bladder surgery highlighted the detailed anatomy of the extra hepatic biliary system. Thus the anatomy of the cystic duct, biliary duct and common bile duct as well as the cystic artery was clearly visualised.
Feedback from the students regarding the effectiveness of this presentation as a means of enhancing the understanding of the normal anatomy of the abdomino-pelvic cavity was obtained by means of a questionnaire with four sections. Three were in the form of direct questions on: 1) Appreciation of specific organs; 2) Functional anatomy of some abdominal structures, and 3) General comments on the overall effectiveness of the programme. The students were requested to register their understanding on a five point Likert scale ranging from ‘Not at all’ to ‘Excellently well’. In the fourth part of the questionnaire, students provided written comments on the programme itself. The responses were analysed and the data are presented below.

Results

The majority of students felt that this teaching paradigm had broadened their perspective (excellent = 51%), had contributed to different areas of study (excellent = 56%), and had improved the quality of the module on the abdomen and pelvis (excellent = 57%) [Figure 1]. As to their ability to appreciate the individual structures, students also had a very positive response, with outcomes of ‘very well’ or ‘excellently well’ for all 16 structures in the video. Particularly high scores were given for the structures of concern in this surgery with the vast majority of students considering them as ‘very well’ or ‘excellently well’ appreciated, for example liver (89%) and gall bladder (85%). Figure 2 shows the composite responses for the groups of structures involved at the site of surgery, the structures seen during the ‘laparoscopic excursion’ and the examples of ‘living anatomy’. Of particular importance was the opportunity for students to see ‘living anatomy’ in the case of peristalsis of the intestines (excellent = 58%), pulsation of the mesenteric arteries (excellent = 27%) and peristalsis of the ureter (excellent = 39%). The complete set of responses can be seen in Table 1.

The written feedback from students was very supportive of these findings. Forty of the 84 students (48%) provided written feedback. Content analysis on the responses to these open questions revealed four main content categories. The most common was the general theme of “thank you” or “it was very good”. The next most frequent content category was comments requesting that laparoscopic video teaching be used more frequently in the course and repeated in the future (45% of respondents). The third content category was that the activity had provided them with clear insight into functional anatomy in a living patient (40% of respondents). The final category was that the activity had helped them to understand the relative positions and spatial relations of the various structures better (23% of respondents). In addition to these four main categories which emerged from the content analysis, there was a variety of individual comments, for example that the activity “provided some variety” to the usual didactic teaching and that the activity “was motivating”. One of the most insightful comments was that this “was the only time there has been complete silence in the lecture hall”.

Discussion

This programme provided the preclinical students with the opportunity to observe in situ the live position and spatial relations of abdominopelvic
Laparoscopic Surgery Recording as an Adjunct to Conventional Modalities of Teaching Gross Anatomy

Additionally, the students could visualise the peristalsis of the intestines and the ureter and the pulsations of the arteries thus appreciating the dynamic anatomy of these regions. Routine cadaveric dissections do not offer the unique aspects which this programme provides to the learner.

The conventional method of teaching anatomy through cadavers, either by dissections or prosections, helps them to understand the inter-relationships of the structures. Nevertheless, it does not give the learner the correct concept regarding the nature and appearance of these structures as living structures. In the conventional learning setting, the preclinical students must wait until they begin their surgery rotation before getting the opportunity to appreciate this all-important aspect of the human body. In the present context, an exposure to the annotated video-surgery has provided these students with the opportunity of appreciating the clinical relevance of the details of anatomy that are learned during the course of human structure. In this respect, this programme has achieved the goals of present day teaching of anatomy, as spelt out by Shaffer.1 To our knowledge, laparoscopic surgery has not previously been used in an organised way to augment the learning outcomes of preclinical students.

It is clear that students rated this exercise very highly as is reflected by both their numeric responses and their written feedback. This programme broadened their perspective and improved their learning of the anatomy of the abdomen as well as enhancing the quality of the module. The written comments of students were very supportive of the use of laparoscopic surgery recordings. Invariably all of them appreciated the efforts taken to show them the video where they could ‘peek into’ the abdominal cavity of a patient. Many of them wanted to see videos of other anatomical areas during their course on human structure as it would help them to appreciate living anatomy better.

In the past, attempts have been made to review the anatomical knowledge of clinical trainees using laparoscopy on embalmed cadavers.5,9,10 Although those learners had the privilege of developing dexterity using the tools on the cadaver, the programme lacked the effects achieved by viewing the live organs in situ, which is attained through the video demonstration of a surgical procedure.

Table 1: Student responses for each item in the questionnaire

<table>
<thead>
<tr>
<th>Structure/Item</th>
<th>not at all</th>
<th>fairly well</th>
<th>well</th>
<th>very well</th>
<th>excellently well</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structure at the site of surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>0</td>
<td>1</td>
<td>8</td>
<td>30</td>
<td>45</td>
</tr>
<tr>
<td>Gall bladder</td>
<td>1</td>
<td>2</td>
<td>10</td>
<td>21</td>
<td>50</td>
</tr>
<tr>
<td>Cystic duct</td>
<td>5</td>
<td>3</td>
<td>19</td>
<td>22</td>
<td>32</td>
</tr>
<tr>
<td>Stomach</td>
<td>1</td>
<td>2</td>
<td>9</td>
<td>24</td>
<td>45</td>
</tr>
<tr>
<td>Coils of the intestine</td>
<td>11</td>
<td>12</td>
<td>15</td>
<td>19</td>
<td>24</td>
</tr>
<tr>
<td>Appendicitis pipiloicae</td>
<td>9</td>
<td>9</td>
<td>15</td>
<td>22</td>
<td>23</td>
</tr>
<tr>
<td>Taneai coli</td>
<td>9</td>
<td>9</td>
<td>15</td>
<td>22</td>
<td>23</td>
</tr>
<tr>
<td>Ascending coli</td>
<td>5</td>
<td>6</td>
<td>16</td>
<td>26</td>
<td>26</td>
</tr>
<tr>
<td>Vermiform appendix</td>
<td>9</td>
<td>6</td>
<td>6</td>
<td>26</td>
<td>34</td>
</tr>
<tr>
<td>Cecum</td>
<td>5</td>
<td>5</td>
<td>13</td>
<td>22</td>
<td>26</td>
</tr>
<tr>
<td>Transverse colon</td>
<td>5</td>
<td>6</td>
<td>14</td>
<td>26</td>
<td>27</td>
</tr>
<tr>
<td>Sigmoid colon</td>
<td>10</td>
<td>12</td>
<td>12</td>
<td>27</td>
<td>18</td>
</tr>
<tr>
<td>Structures seen on ‘laparoscopic excursion’</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>15</td>
<td>5</td>
<td>12</td>
<td>26</td>
<td>20</td>
</tr>
<tr>
<td>Fallopian tube</td>
<td>7</td>
<td>8</td>
<td>6</td>
<td>27</td>
<td>33</td>
</tr>
<tr>
<td>Ovary</td>
<td>7</td>
<td>7</td>
<td>5</td>
<td>28</td>
<td>31</td>
</tr>
<tr>
<td>Falciform ligament</td>
<td>10</td>
<td>13</td>
<td>9</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>Living anatomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peristalsis of the intestines</td>
<td>2</td>
<td>5</td>
<td>6</td>
<td>18</td>
<td>49</td>
</tr>
<tr>
<td>Pulsation of the mesenteric arteries</td>
<td>10</td>
<td>14</td>
<td>15</td>
<td>14</td>
<td>23</td>
</tr>
<tr>
<td>Peristalsis of the ureter</td>
<td>9</td>
<td>12</td>
<td>9</td>
<td>13</td>
<td>33</td>
</tr>
<tr>
<td>Student’s views of the video</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Broadens your perspective</td>
<td>0</td>
<td>0</td>
<td>8</td>
<td>32</td>
<td>41</td>
</tr>
<tr>
<td>Contributes to different areas of study</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>29</td>
<td>45</td>
</tr>
<tr>
<td>Improves quality of the module</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>26</td>
<td>45</td>
</tr>
</tbody>
</table>
Academic use of laparoscopic surgery recordings has previously been restricted to those used for training surgeons and quite often these procedures have been performed on laboratory animals in an effort to impart the techniques and dexterity to the surgeons in the making. The possibility of using laparoscopic recordings for academic purposes was suggested in a review article, but so far there have been no reports of their organised use in an academic setting for preclinical medical training.

Nowadays, there is a need to use innovative teaching methods to instill enthusiasm and positive learning attitudes in students. Videos of laparoscopic procedures, a valuable teaching resource, can be obtained without inconveniencing the patient since almost all such procedures are routinely recorded by surgical teams; it therefore requires neither extra time and effort nor any additional cost. Routinely recorded surgeries can be used in emphasising the spatial relationship of organs. Moreover, exposure to such surgical procedures enables the preclinical students to appreciate the relevance of anatomy learnt during the course of human structure to the practice of clinical medicine. Such awareness renders the learning process more useful and meaningful. This learning experience also provides an opportunity early in their career, for students to consider their future speciality and the field for their residency programme. Overall, this programme has proved to be a useful adjunct to the conventional method of learning morphological sciences.

The entire course content of the anatomy of abdomen and pelvis cannot, however, be taught through laparoscopic videos alone. It is understood that these videos, when properly used, become a valuable adjunct to the conventional teaching of gross anatomy, enhancing the appreciation of living anatomy of the region. It should be possible to choose appropriate laparoscopic surgery recordings to supplement the understanding of the anatomy of specific areas such as: laparoscopic cholecystectomy, herniorrhaphy, appendectomy, salpingectomy, and removal of the fibroids from the uterus. Recordings of such surgeries are available on the Internet and could be readily used to supplement conventional teaching; however, the video used in the present context was unique since it was specifically recorded to enhance the learning of preclinical students. It amply served its purpose.

With the advent of recent technological advances in the field of medicine, it becomes necessary for medical educators to equip the students with tools for self-directed learning. This will help them to keep pace with the current trends in clinical sciences and to stay abreast of the developments in continuing medical education once they graduate.

Conclusion

The students’ responses in the present study were positive enough to recommend that selected videos of laparoscopic procedures be used more widely in order to make the teaching of anatomy more interesting and relevant to clinical medicine. Encouraged by this experience, it is tempting to suggest that this modality of teaching may be incorporated as a standard element into the preclinical academic programme.

Conflicts of interest

The authors reported no conflict of interest.

Acknowledgement

We gratefully acknowledge the help of Dr P. Vasudevan, Consultant Laparoscopic Surgeon, Coimbatore, India, who provided us with the recording of laparoscopic surgery that was used in this research.

References


Nephropathic Cystinosis
First reported case in Oman

Dana Al-Nabhani,1 *Mohammed El-Naggari,1 Rana Al-Sinawi,1 Alexander P. Chacko,1 Anuradha Ganesh,2 Ibti Sam El Nour1

Cystinosis is a lysosomal storage disease that is inherited in an autosomal recessive manner. Cystinosis, which is a lysosomal transport molecule needed to carry cysteine out of the cells, is defective in this disease. This leads to the intracellular accumulation of the amino acid cystine in different organs and tissues. It is a multisystemic disease that can present with renal and extra renal manifestations. There are three types of cystinosis, infantile nephropathic cystinosis being the most severe form. In this report we present the classic clinical features of nephropathic cystinosis in an Omani child. This condition remains quite rare in the Middle East and is the first reported case of nephropathic cystinosis in the Omani population.

Keywords: Cystinosis; Fanconi syndrome; Lysosomal storage disease; Cysteamine; Crystals; Case report; Oman.

Case Report
A 21-month-old Omani girl was referred to Sultan Qaboos University Hospital for evaluation of severe failure to thrive. This was the second child born to first degree consanguineous parents at full term by spontaneous vaginal delivery. Her birth weight was 2.8 Kg. According to the parents she was doing well until the age of 7 months, when she was noted by the primary care physician to be below the 3rd centile for both weight and height. At that point, it was felt that the failure to thrive was nutritional, since her mother gave history of exclusive breast feeding until the age of 7 months. Despite the nutritional advice and nutritional support for several months, the child did not gain weight and was referred to the Department of Child Health at Sultan Qaboos University Hospital at the age of 21 months with a weight of 5.36 Kgs. The mother gave a history of polyuria, which was suggested by the fact that she had 10 wet diapers per day, polydipsia and
constipation since the age of 18 months. She had a voracious appetite. Developmentally, she was able to sit without support; however, she needed support for standing and walking. She had appropriate social development for her age. The family history was negative for similar conditions and for any renal or metabolic diseases. Also there was no history of miscarriages. On physical examination, the child was dark skinned, identical to her parents’ skin complexion. Her growth parameters were as follows: height 66 cm, weight 5.36 Kg, which are both below the 5th percentile; the head circumference was 45.5 cm which was normal for her age. She did not have any dysmorphic features. She had frontal bossing and sparse, thin hair. She also had wide wrists, rachitic rosary, double malleoli and genu valgum. The abdomen was protuberant without organomegaly. The cardiovascular and respiratory examinations were normal. The initial blood investigations are summarised in Table 1. Urinalysis was positive for glucose (+2) and protein (+1). The urine pH was 5, the specific gravity was 1.010 and the urine anion gap was positive. Urine reducing substances were negative. Urinary amino acid tests were done and showed significant elevation of all measured amino acids with the exception of aspartic acid, methionine, 1-methylhistidine, and turine. An indirect clue of this was the significantly elevated protein to creatinine ratio 106 mg/mmol (normal <50 mg/mmol) with mild proteinuria in the dipstick. The tubular reabsorption of phosphate was 55% (normal > 85%).

Table 1: Results of the initial blood investigations

<table>
<thead>
<tr>
<th>Test</th>
<th>Patient result</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>132 mmol/L</td>
<td>135–145 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.1 mmol/L</td>
<td>3.5–6.1 mmol/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>105 mmol/L</td>
<td>98–107 mmol/L</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>17 mmol/L</td>
<td>22–29 mmol/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>16 umol/L</td>
<td>15–31 umol/L</td>
</tr>
<tr>
<td>Urea</td>
<td>1.6 mmol/L</td>
<td>2.1–7.1 mmol/L</td>
</tr>
<tr>
<td>Anion gap</td>
<td>10 mmol/L</td>
<td>5–13 mmol/L</td>
</tr>
<tr>
<td>Total calcium</td>
<td>2.42 mmol/L</td>
<td>2.17–2.55 mmol/L</td>
</tr>
<tr>
<td>Corrected Calcium</td>
<td>0.64 mmol/L</td>
<td>2.1–2.55 mmol/L</td>
</tr>
<tr>
<td>Phosphate</td>
<td>0.58 mmol/L</td>
<td>1.16–2.10 mmol/L</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>841 units/L</td>
<td>0–281 units/L</td>
</tr>
<tr>
<td>Albumin</td>
<td>46 g/L</td>
<td>38–54 g/L</td>
</tr>
<tr>
<td>Parathyroid hormone</td>
<td>2.1 pmol/L</td>
<td>1.6–9.3 pmol/L</td>
</tr>
<tr>
<td>25-OH Vitamin D</td>
<td>55 nmol/L</td>
<td>22.5–91.8 nmol/L</td>
</tr>
<tr>
<td>1,25 Vitamin D</td>
<td>45 pmol/L</td>
<td>40–140 pmol/L</td>
</tr>
</tbody>
</table>

A wrist X-ray was obtained in view of the physical findings. This showed reduced bone density, widened metaphysis of the ulna and radius with cupping and fraying. No carpal bones were noted and the bone age was delayed [Figure 1]. An abdominal ultrasound was also obtained and this showed normal intra-abdominal organs including two normal kidneys. She also underwent an ophthalmic examination that revealed normal visual acuity in both eyes. No strabismus, nystagmus or ocular motility disturbance was noted. However, slit lamp examination of the anterior segment of both eyes revealed fine, shiny crystal-like deposits diffusely distributed in the corneal epithelium and stroma. The surface of the epithelium was intact and the rest of the examination was unremarkable. The fundus examination showed no abnormal morphology of the disc, macula and vessels and a normal retinal background. With the presence of failure to thrive in a child with renal tubular acidosis and features of Fanconi syndrome, the ophthalmic findings of crystals in the cornea led to the diagnosis of cystinosis [Figure 2]. Retinopathy is usually a late finding of this condition and not seen in early childhood; it is preceded by corneal crystals.

The child was started on supportive treatment

Figure 1: Patient’s wrist X-ray showing reduced bone density, widened metaphysis of the ulna and radius with cupping and fraying.
Case Report

which included potassium citrate to correct the metabolic acidosis and hypokalemia, calcium sandoz, phosphate sandoz and alfacacidol. Calcium was given for the severe hypocalcaemia. Also phosphate supplements were indicated due to severe hypophosphatemia. To avoid the risk of precipitation, a gap of at least four hours was left between each dose of the supplements. With this supportive treatment her weight increased to 7.2 kg and she was able to progress on her motor development milestones. Cysteamine, which is a cystine depleting agent and the mainstay treatment for this disease, had to be ordered since it had never been used before in Oman. She was started on cysteamine 50 mg orally every 6 hrs (30 mg/kg/day) as soon as the medication was available. The aim was to increase the dose slowly to reach 50 mg/kg/day over 4-6 weeks.

Discussion

There are different types of cystinosis: the nephropathic and non-nephropathic. The nephropathic type has renal and extra renal manifestations. This can present in an infantile or late onset form. The infantile form is the most severe and, if left untreated, can lead to end stage renal disease by late childhood. The non-nephropathic type presents with photophobia and only corneal cystine crystals without renal or systemic involvement. This type is also called ocular cystinosis.

Children with the infantile form appear normal at birth. The clinical picture becomes apparent between 3 and 6 months of age. The most common renal manifestation is the renal Fanconi syndrome due to renal proximal tubular dysfunction. This classically presents with failure to thrive, polyuria up to 2–3 litres/day, polydipsia, constipation, dehydration, weakness and hypophosphatemic rickets. Patients will also have glucosuria, proteinuria, phosphaturia, aminoaciduria and metabolic acidosis.

Our patient presented at the age of 7 months with failure to thrive and had the classic features of renal Fanconi syndrome such as polyuria, polydipsia and constipation. She also had signs of rickets clinically, biochemically and radiologically. The laboratory investigations were also classic for renal Fanconi syndrome: normal anion gap, metabolic acidosis with hypokalemia and hypophosphatemia. She also had evidence of renal wasting of glucose which was suggested by normal serum glucose and a positive dipstick for glucose. The protein to creatinine ratio was quite elevated despite normal albumin and minimal proteinuria on dipstick. This suggests that the proteins lost are low molecular weight amino acids rather than the albumin which is a large molecular weight protein. She also had evidence of renal phosphate wasting suggested by hypophosphatemia and low tubular reabsorption of phosphate which was 55% (less than 85% indicates renal wasting).

The other manifestations of nephropathic cystinosis are extrarenal and present later on. These include myopathy and dysphagia due to accumulation of cystine in the muscles, endocrine involvement such as hypothyroidism and diabetes mellitus, hepatomegaly, hypersplenism and photophobia from the corneal accumulation of cystine in the cornea. Fundoscopy may show depigmentation of the retina. Retinal changes may appear before the corneal features. The corneal crystals require slit lamp examination. These crystals are not present at birth; they appear between 16 and 20 months of age. The corneal crystals are virtually pathognomonic. However, their absence does not exclude the diagnosis of cystinosis. Our patient had the typical crystal deposits in the cornea as seen in Figure 2.

Nephropathic cystinosis is the most common cause of renal Fanconi syndrome in the Caucasian population. This disease is quite rare in the Middle East. Only three Middle Eastern countries, Egypt,
Saudi Arabia and Iran, have reported this disease in their populations.3,5 These studies have provided a lot of important information on nephropathic cystinosis in the region. Soliman et al., in the Egyptian study, were able to identify 16 patients with nephropathic cystinosis out of 33 who presented with Fanconi syndrome to a single centre.3 The Saudi study, by Aldahmesh et al., identified 8 mutations, 4 of which were novel, in 21 patients with nephropathic cystinosis of Arab origin.5 The Iranian study by Mirdehghan et al. described the clinical features of patients with nephropathic cystinosis presenting over a five year period to a single centre.4

The diagnosis of nephropathic cystinosis in this case was based on the presence of corneal cystine crystals in an infant with Fanconi syndrome. Traditionally, white blood cell cystine assay was the test of choice to confirm the diagnosis. This test is not available in Oman and it is costly and technically difficult to perform; there are only a few laboratories worldwide that can perform it. Currently, genetic testing by mutation analysis of the CTNS gene is a better alternative to confirm the diagnosis. It is necessary to consider sending samples to a specialised laboratory in case the diagnosis of nephropathic cystinosis is suspected in an infant younger than 20 months where the cystine crystals might not be present. Early treatment with cysteamine which is a cystine depleting agent can delay the progression to end stage renal disease.

**Conclusion**

Given the high consanguinity rate in the Omani population, nephropathic cystinosis should be considered in any child presenting with Fanconi syndrome. Immediate referral to a tertiary hospital with nephrology and ophthalmology services is important to avoid delay in treatment.

**References**

Acutely fatty liver of pregnancy (AFLP), a life threatening obstetric emergency, was first described by Sheehan in 1940. The most common presentation is malaise, nausea, vomiting and epigastric pain followed by jaundice. Due to high maternal and perinatal mortality, early diagnosis, prompt delivery and supportive care are required. We report an atypical case of AFLP and discuss the management and complications of this rare obstetric disorder.

**Keywords:** Acute fatty liver of pregnancy; Postpartum haemorrhage; Disseminated intravascular coagulation; Case report; Oman.

**Case Report**

A 36 year-old healthy woman, gravida 3 para 2, presented to a peripheral hospital at 34 weeks gestation with a 3-day history of malaise, nausea, vomiting and abdominal pains. Her pregnancy had been uncomplicated. On admission, her vitals appeared to be stable, but her blood pressure was 150/90 mmHg with no proteinuria. The results of the complete blood count was as follows: haemoglobin 13.4 g/dl; white blood count 22 × 10^9/L, and platelets, 227 × 10^9/L. The biochemical markers were as follows: total bilirubin 122.8 µmol/L; serum aspartate aminotransferase (AST) 118.9 IU/L; serum alanine aminotransferase (ALT) 129.8 IU/L, and creatinine 158.5 µmol/L. The coagulation profile was as follows: prothrombin time (PT) 13 sec; activated partial thromboplastin time (APTT) 41 sec.

The patient underwent an emergency caesarean section because of a non-reassuring fetal heart tracing. The outcome was a live male baby with good Apgar scores. The next day, the patient started bleeding profusely through the vagina and her haemoglobin dropped to 4.9 g/dl; the platelet count was 25 × 10^9/L and fibrinogen 0.5 g/L. She was assessed, but no cause of bleeding identified. She was taken to the operating room and an exploratory midline laparotomy was performed. No
source of bleeding was identified intraoperatively and the abdomen was packed, closed and an intraperitoneal drain was inserted. A hysterectomy was not performed and no other intervention was done.

The patient was then transferred to the intensive care unit (ICU) at Sultan Qaboos University, tertiary hospital, Oman, after receiving a total of 10 units of packed red blood cells, 19 units of fresh frozen plasma, 7 units of cryoprecipitate and 7 units of platelets. She was ventilated and was on intravenous dopamine infusion. The patient was bleeding profusely from her intraperitoneal Jackson-Pratt (J-P) drain. The laboratory findings on admission at our hospital were as follows: Hb 12.4 g/dl; platelets 56 x 10^9/L; PT 23 sec; APTT 40 sec; fibrinogen 1.5 g/L; total bilirubin 155 µmol/L; AST 123 IU/L; ALT 123 IU/L, and creatinine 163.9 µmol/L. The patient required further replacement of blood products. At our hospital, she received a total of 5 units of packed red blood cells, 5 units of fresh frozen plasma, 11 units of cryoprecipitate and 10 units of platelets. Two units of recombinant activated factor VII (rFVIIa) were given to her and the bleeding lessened thereafter. She was taken to the operating room 24 hours after admission for removal of the abdominal packs. At the time of surgery, it was noted the abdominal packs were foul smelling and adherent to the serosal layers. The abdominal wall was bruised, but no active bleeding was observed. Since there was no active bleeding, a hysterectomy was not performed, the packs were removed and abdomen was irrigated well and closed in layers. During the patient’s ICU stay, she was on intravenous labetalol infusion for 48 hours to control her blood pressure. She was extubated on day 4 and moved to the ward on day 8 of admission.

The patient’s status improved gradually, but she remained severely jaundiced with high bilirubin levels, mainly of the conjugated type (maximum total bilirubin level of 280), raised liver enzymes remaining in the hundreds and hypoalbuminemic (15 g/dl). Viral hepatitis screening was done, but was negative. The dilemma was the amount of serous fluid drainage, first from the J-P drain that was removed on day 8 of admission and then from the patient’s wound site. Clinical assessment and several investigations were performed including creatinine levels of the draining fluid, intravenous pyelogram, and ultrasound and computed tomography (CT) scans of the abdomen that excluded wound dehiscence, urinoma and seroma. On the bases of her clinical presentation including her signs, symptoms, massive bleeding and laboratory findings, the diagnosis of AFLP was made and supportive care continued. Further investigations with liver ultrasound and CT scans did not show evidence of fatty changes of the liver and a liver biopsy was not performed.

On day 18 of admission, the patient was febrile and her wound grew a *Pseudomonas* species infection that was treated with intravenous antibiotics (meropenem). On day 21 of admission, complete wound dehiscence was found and an emergency surgery was performed. It was noted during the surgery that there were lots of adhesions, the liver was frozen with multiple adhesions, the bowel was inflamed and the rectus fascia was not healthy. After adhesiolysis and extensive washing of the abdominal cavity with normal saline, a mass closure of the abdomen was performed using tension sutures. Postoperatively, the patient did well. The wound healed with the assistance of the vacuum assisted closure (VAC) system. The sutures were removed after 4 weeks and she was discharged home. She was monitored closely in the outpatient clinic and on her six weeks follow-up, the liver enzymes, bilirubin and albumin levels were normal and she was off antihypertensive medications.

**Discussion**

Hypertensive and liver disorders of pregnancy comprise a spectrum of conditions associated with adverse fetomaternal outcomes. The patient’s initial presentation may vary during the antepartum, intrapartum and even the postpartum period. Clear understanding of the pathophysiology and mechanism of these disorders in pregnancy is very important. Although severe preeclampsia is commoner than AFLP and other liver disorders related to pregnancy, our patient’s presentation and laboratory test results were in favour of an AFLP diagnosis. Ch’ng et al. first set the Swansea criteria for diagnosing AFLP that have been used by many institutions. Six or more of the following features are used to diagnose AFLP in the absence of other explanation: vomiting; abdominal pain; polydipsia/polyuria; encephalopathy;
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Elevated bilirubin >14 µmol/L; hypoglycaemia <4 mmol/L; elevated urate >340 µmol/L; leukocytosis >11x10⁹/L; ascites or bright liver on ultrasound; elevated transaminases; elevated ammonia >47 µmol/L; renal impairment creatinine >150 µmol/L; coagulopathy (PT >14 sec or APTT >34 sec), or microvesicular steatosis on liver biopsy. Using these criteria we anticipated the diagnosis of AFLP. The patient had vomiting, abdominal pain, elevated bilirubin and transaminases, elevated creatinine and coagulopathy at presentation. A patient with severe preeclampsia/HELLP will usually present with proteinuria.

AFLP was first described by Sheehan in 1940. The aetiology of the disease is unknown with an incidence of 1 in 10,000 to 1 in 15,000. It is a life threatening obstetrical emergency that can lead to high maternal and perinatal morbidity and mortality. Due to the development of more rapid diagnosis tools and early termination of pregnancy, the maternal mortality rate due to this disease has decreased from 80–85% to 7–18% and the fetal mortality rate from 50% to 9–23%. The disease usually presents in the first pregnancy and in the third trimester with a mean gestational age of 34–37 weeks. The signs and symptoms at initial presentation may vary, making the diagnosis of this disease difficult, or there might be delay in diagnosis. Similarly, the differential diagnosis may be difficult in a patient with abnormal hepatic function in pregnancy since a number of pathologies such as HELLP syndrome, viral hepatitis and hormone-induced cholestasis share some of the same symptoms and signs.

The diagnosis of AFLP remains challenging since there is no specific non-invasive diagnostic test to identify it. Ultrasound and CT scans of the liver have been used, but the specificity and sensitivity of these studies are insufficient to make a diagnosis and the likelihood of false negative results is high. Our patient had normal liver ultrasound and CT scan results.

Liver biopsy is the gold standard test, but it is invasive and requires a patient with normal coagulation status. The clinical presentation of both AFLP and HELLP syndrome are very similar but nausea, vomiting, epigastric pain and jaundice are more commonly seen in AFLP patients. Although AFLP is an uncommon disease, our patient’s presentation and the development of jaundice with chronic hypoalbuminemia made this diagnosis more likely. Moreover, the patient developed DIC requiring massive blood transfusion (total of 76 units), making the diagnosis of AFLP more likely. DIC is seen in about 80–100% of patients with AFLP as opposed to 21% of patients with HELLP syndrome. The DIC might be a severe and potentially fatal complication of AFLP. The main cause of the coagulopathy leading to DIC in patients with AFLP is the severe hepatic dysfunction. It is less likely to be a complication for patients with other obstetrical or medical disorders such as HELLP syndrome. Early identification and correction of the coagulopathy before any obstetrical procedure is very important. When the patient presented to our ICU, after having two surgeries within 24 hours, it was very difficult to make the decision to take her back to the operating room to control her bleeding. We continued replacing her with blood products and decided to give her rFVIIa and observe if the latter would control the bleeding. Fortunately, the bleeding settled and the patient stabilised after receiving two doses of rFVIIa.

There are an increasing number of case reports in the literature describing the successful “off-label” use of rFVIIa (NovoSeven, Novo Nordisk, Denmark) in the treatment of massive postpartum haemorrhage (PPH) refractory to conventional medical and surgical therapy. The rationale for the use of rFVIIa in this setting is based on the observation that it directly activates factor X on the surface of activated platelets at the site of injury, factors VIII, and IX. This results in a “thrombin burst” with the conversion of prothrombin into large amounts of thrombin and the local formation of a stable fibrin clot that may control bleeding. A recent systematic review was undertaken by a group in Italy looking at the effects and role of rFVIIa in patients with massive PPH. Nine studies met the inclusion criteria and there were 272 patients involved. The group made the following recommendations: 1) Consider the use of rFVIIa in cases of massive PPH refractory to medical therapy including replacement of other blood products and even after a conservative/invasive surgical approach such as internal iliac or uterine artery ligation fails; 2) Consider a second dose of rFVIIa (90 mg/kg IV bolus over 3–5 min) if there is no response after 20 minutes from the first dose, and 3) If bleeding
persists after 2 doses of rFVIIa, consider performing a hysterectomy.

Conclusion
Despite the critical condition at presentation, and the complications she went through such as DIC, chronic hypoalbuminemia, infection and burst abdomen, our patient finally went home in a good condition. Early diagnosis of obstetrical emergencies, prompt therapy, adequate supportive care and a multidisciplinary approach are the key elements for a good outcome.

Acknowledgement
I wish to thank all the staff at Sultan Qaboos University Hospital, especially those in the blood bank, for all their support and efforts in this case.

References
Cannabis is the most widely used illicit drug in many developed societies. It is estimated in the USA that the population incidence rates of marijuana use from late childhood to adolescence increase from 1.30% to 16.29% from age 11 to 16 years, and then appear to plateau. A sharp increase is noted during ages 13–15 years.1 There is a paucity of statistics about the prevalence of cannabis use in Oman; however, the government has recently established a new 50 bed psychiatric hospital specialised in the treatment of addiction. Absolute numbers from 1994 indicate that 150 people were addicted to cannabis (hashish) and, in 2009, 19 people died of drug abuse.2

According to botanical classification, cannabis comes from family of Cannabaceae and species of *stiva, indica* and *ruleralis*.3 The common names for cannabis are: marijuana, marihuana, potweed, grass and Mary Jane.3 There are multiple risks from using cannabis, e.g. decreased ability to concentrate, decreased motivation, balance problems, increased heart rate and blood pressure, damage to fertility and increased risk of serious psychiatric illness.4 Behavioural problems were associated with early marijuana use specifically in those who started to use cannabis prior to 15 years of age.5 Recent cannabinoid research discovered an endocannabinoid system with specific genes coding for cannabinoid receptors (CBRs).6 The availability of these endocannabinoids in breast milk can affect the development of the newborn baby.6

**Abstract:** We report a confirmed case of cannabis exposure in an Omani female child with developmental delay. Cannabis exposure in children can lead to many consequences; for example, chronic use can result in developmental delay, abnormal behaviour, and hyperactivity while there is a risk of coma with acute exposure. It is important for clinicians to consider substance abuse as a differential diagnosis for similar presentations in paediatric patients, noting that children are at risk of cannabis exposure if their parents/caregivers are cannabis users.

**Keywords:** Cannabis abuse; Child abuse; Child development; Developmental delay disorders; Case report; Oman.
Cannabis Exposure in an Omani Child
First case report from Oman

heroin, cocaine, methamphetamine, and other drugs expose children to risk in multiple ways. Members of the medical community need to understand these risks, and be aware of the consequences on children in the care of adult abusers. The misuse of drug substances by children may have far-reaching consequences, and may impact family unit functions. Many substance abusers are polysubstance users leading to a compounded negative effect which may be difficult to measure. Often, other interrelated social factors, such as untreated mental illness, alcoholism, trauma history and domestic violence also affect these families.7

There are several paediatric case reports found in the literature regarding cannabis abuse/exposure leading to effects on cognitive function/behavior and coma, but none specifically on cannabis exposure in children in Oman.8,9 This case report describes illicit cannabis exposure in an Omani female child with developmental delay.

Case Report
An Omani female child, aged 2 years and 10 months, was brought by her parents to the Accident and Emergency Department of Sultan Qaboos University Hospital, Muscat, Oman. The patient presented with drowsiness, abnormal eye movements, was lethargic and had been unable to sit or stand for the previous 4 hours. The history was reluctantly provided, so the physician on call documented the unconfirmed information given by the parents, noting that it was somewhat inconsistent in nature. The father made little eye contact with medical personnel, and seemed uncomfortable. His verbal and non-verbal expressions and cues to his wife indicated that she was not to offer any information. Apparently, the patient had ingested an unknown blackish substance mixed with sand, followed by vomiting, further lethargy and drowsiness, with nystagmus. The parents sought medical assistance approximately 4 hours after the onset of symptoms. Of note, the child's chart indicated that she had been a full term baby. However, there had been a delay in gross motor skill and language development noted to have begun at approximately 2 years of age. The parents indicated that the patient was a hyperactive child who occasionally ate her own hair. The physician noted that the family as a unit presented with psychosocial and alcoholism/substance issues, and loss of income. It was noted that two older siblings were "normal" as indicated by the mother of the patient.

On initial examination, the following parameters were significant: lethargy, drowsiness, Glasgow coma scale of 12/15, tachycardia, nystagmus, and pupils dilated (4 mm), but reactive to light. A gastric lavage was performed, producing gastric aspirate mixed with food particles. During this procedure, the child vomited a blackish sticky substance, with subsequent clinical improvement over the ensuing hours. The samples were sent for analysis, and she was hydrated intravenously. Investigations revealed microcytic hypochromic anaemia while all other investigations were normal. The patient rested through the night, and continued to improve. The subsequent plan was to involve social work and perform an HIV test, but the patient's father discharged her against medical advice. An incident report indicating suspected child abuse was filed. Five days later, tetracannabinoid substance was confirmed in the child's vomit.

Discussion
Children exposed to maternal addiction have increased rates of cognitive, socio-emotional, and behavioural problems.10 This case report illustrates an Omani female child who was exposed to cannabis. The child was noted to have developmental delay and hyperactivity to which prenatal/chronic cannabis exposure may have been a contributing factor. A prospective investigation showed that there is a significant association between substance use disorder in parents and cannabis use disorder and behavioural disinhibition in their sons.11 The Generation R study showed that multiple demographic, emotional and social characteristics were associated with maternal cannabis use. These characteristics should be considered when investigating offspring exposed to cannabis in utero as they may be important in mother-child interaction and child development.12 There is indirect evidence of post-pregnancy resumption of substance use. Pregnant and parenting women, regardless of race or ethnicity, benefit from prevention efforts focusing on cessation rather than temporary abstinence from substance use.13
This patient demonstrated speech delays and hyperactivity, which were also found in one case report in which a Californian teacher of a 7 year-old boy, who had been exposed prenatal to cannabis, noted that he demonstrated frequent fidgety behaviour, hyperactivity, and trouble focusing on learning tasks. Noted by family to be a "sweet and happy" child at home, his parents still expressed concern about his repetitive behaviours, fear of leaving the house, and insistence on a certain order of his toys. He also displayed "meltdowns" and tantrums at non-compliance with his wishes. A receptive and expressive language disorder had previously been diagnosed at 4 years of age, and been followed by speech therapy and a social skills language group programme.

Survival analysis in another study revealed that aggressive, co-morbid, and inattentive/hyperactive schoolchildren had a significantly earlier onset of drinking, drunkenness, marijuana and overall illicit drug use compared to healthy schoolchildren. The conclusions of this study were as follows: three levels of behavioural risk of substance abuse exist: 1) the highest level has trajectories of increased aggressive and inattentive/hyperactive problems throughout childhood; 2) the next level involves only an increased inattentive/hyperactive behavioural trajectory, and 3) the lowest level involves those with neither type of problem. Children with both inattention/hyperactivity and aggression have the greatest need for childhood intervention to prevent substance abuse in adolescence. Emerging evidence from human studies and animal research demonstrates that an early onset of cannabis consumption might have lasting consequences on cognition; may increase the risk of neuropsychiatric disorders, promote further illegal drug use, and increase the likelihood of cannabis dependence. These findings suggest that young people represent a highly vulnerable cannabis consumer group, carrying a higher risk than adult consumers of suffering adverse consequences from cannabinoid exposure.

There are four independent factors in early or middle childhood that predict early initiation of use of substances and subsequent substance use disorders by early adulthood: 1) Disrupted families or drug-using parents 2) Problem behaviours; 3) Poor parental monitoring, and 4) Poor parental supervision. The father of this patient had no consistent employment, possibly partly due to cannabis abuse. High levels of cannabis abuse are related to poorer educational outcomes, lower income, greater welfare dependence and unemployment, and lower relationship and life satisfaction.

Conclusion

It is important for clinicians to consider substance abuse as a differential diagnosis for presentations similar to this case in other paediatric patients. Emergency medicine clinicians should be able to detect suspicious behaviour as described above, supported by inconsistent information/history given by family members in order to provide appropriate immediate treatment, and also initiate follow-up care for the patient and possibly also for the family.

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References


Prior to the advent of laparoscopy, laparotomy and open repair of intraperitoneal bladder injuries was thought to be necessary in all cases. Laparoscopic surgery offered new possibilities in treating traumatic intraperitoneal bladder ruptures. Laparoscopy as a diagnostic modality in trauma has been reported; however, therapeutic laparoscopy for trauma remains a controversial subject. The reason for the controversy is that laparoscopy might not identify occult small bowel perforation unless it is done by an experienced laparoscopic surgeon who can examine the bowel laparoscopically.

The most common cause of bladder rupture is blunt trauma to the lower abdomen associated with pelvic fractures. Traumatic intraperitoneal bladder rupture is a true surgical emergency managed conventionally by open laparotomy with single layer or double layer repair.

Case report

A 37-year-old driver, who was wearing a seat belt, was involved in a motor vehicle collision and brought by the Emergency Medical Services to the Emergency Department of Sultan Qaboos University Hospital. He had no history of loss of consciousness or vomiting. He complained of severe left hip pain. On physical examination, he was confused with Glasgow Coma Scale 14, but no neurological deficit. He had normal vital signs with blood pressure of 105/60 mmHg, a pulse rate of 63 beats per min and normal oxygen saturation. He had a left periorbital haematoma, multiple abrasions in his face and small lacerated wounds on the left forehead and cheek. His abdomen was distended and tense with multiple small abrasions, but there was no tenderness. He had multiple bruising and abrasions on his lower limbs. His left hip was flexed and medially rotated. An X-ray of the
pelvis showed left hip dislocation with a fractured acetabulum [Figure 1].

A Foley catheter was inserted as there were no signs of urethral injury, and there was gross haematuria. A contrast abdominal computed tomography (CT) scan revealed a moderate amount of free fluid in the abdomen and pelvis with a laceration of the anterior pole of the spleen and a 3 cm liver laceration. The kidneys and ureters were normal. The abdominal CT was followed by a CT cystogram which revealed intraperitoneal extravasation of contrast seen from the bladder [Figure 2]. The posterior dislocation of the left hip and the fracture of the posterior margin of the acetabulum were also identified [Figure 1].

A CT scan of the head showed fractures of the left mandible and zygoma bones, and damage to the pterygoid muscle, and the lateral wall of the left maxillary sinus. The trauma team then planned for an emergency laparoscopic repair of the bladder rupture. During the operation, a three port-technique and a 30-degree angle 10 mm camera were used and the findings were minimal blood collection in the pelvis about 15 ml with a 4 cm bladder rupture at the dome [Figure 3]. The laceration was sutured with a continuous single layer of absorbable suture 2/0 Vicryl. Then the repair was tested by injecting 500 ml of normal saline into the bladder through the Foley catheter; no leak was noticed from the suture line. A drain was then placed in the perivesical space to monitor postoperatively for possible urine extravasation.

The bladder repair was combined with an orthopaedic procedure, where a closed reduction of the left hip dislocation and skeletal traction, using a pin to the proximal tibia, were performed.

Postoperatively, the patient was admitted to the surgical high dependency area. He had a three-way Foley catheter with continuous irrigation until his urine became clear. Daily monitoring of his complete blood count, liver function test, urea and electrolytes revealed normal results. A broad-spectrum antibiotic and low molecular weight heparin, as prophylaxis for deep vein thrombosis, were administered. He was managed in conjunction with the ophthalmologist, and otolaryngological, maxillofacial and orthopaedic surgeons for the associated injuries and treated accordingly. On the 7th postoperative day, a cystogram revealed no leakage, so the Foley catheter and the intraperitoneal drain were removed and he had an uneventful recovery.

**Discussion**

Bladder catheterisation for extraperitoneal perforation and cystorrhaphy for intraperitoneal perforations are well established treatment recommendations for bladder rupture.

Traumatic intraperitoneal bladder rupture always requires surgical exploration and suturing. This type of damage is usually repaired by laparotomy, often because of accompanying
damage to other organs and pelvic bone fractures. In addition, this type of injury does not heal with prolonged catheterisation alone.\textsuperscript{3}

The first case of successful laparoscopic repair of iatrogenic intraperitoneal bladder rupture was reported in 1990. Subsequently, a number of cases using the laparoscopic approach have been reported for the treatment of traumatic, spontaneous and iatrogenic bladder rupture.\textsuperscript{4}

The first case of laparoscopic repair of traumatic intraperitoneal bladder rupture was reported in 1996,\textsuperscript{5} and the first case of laparoscopic repair of idiopathic intraperitoneal bladder rupture was reported in 1997.\textsuperscript{6}

A literature review supports the fact that laparoscopy can be used safely and effectively instead of open laparotomy for the diagnosis and treatment of traumatic abdominal injuries.\textsuperscript{7} Figueiredo et al. found in their case of a 20 year-old female, who suffered ventral collision and a 5 cm bladder rupture in the dome after a fall from the second floor, that in stable patients the laparoscopic approach is a less traumatic treatment allowing visualisation of the entire peritoneal cavity to exclude other lesions and offers the shortest recovery time.\textsuperscript{8} Mikulska-Jovanovic et al. concluded in their report on a 34 year-old male, who suffered blunt lower abdomen injury, that laparoscopy is an effective and timely way to treat this type of injury, gives a favourable cosmetic effect, shortens the time of hospitalisation, and reduces the risk of wound infection after the operation.\textsuperscript{9} This conclusion was corroborated by Kim et al. in their report.\textsuperscript{9} Matsui et al. reported a case of extraperitoneal and intraperitoneal traumatic bladder injury successfully managed with combined endoscopic and laparoscopic procedures.\textsuperscript{10}

Laparoscopy can avoid laparotomy in 63\% of the cases, decreasing its associated morbidity.\textsuperscript{11} As was shown in several studies, there was no difference in outcome between single layer repair\textsuperscript{3,4,8} and double layer repair.\textsuperscript{12,13} In haemodynamically stable patients without diffuse peritonitis, diagnostic laparoscopy is an effective intervention in stab wounds, gunshot wounds with questionable peritoneal penetration and in blunt trauma with free peritoneal fluid or equivocal physical examination.\textsuperscript{8}

### Conclusion

Laparoscopy can be a safe, feasible and effective procedure for the evaluation and treatment of haemodynamically stable patients with abdominal trauma. It can reduce the number of non-therapeutic laparotomies performed. Laparoscopic repair of traumatic intraperitoneal rupture of urinary bladder is an effective and timely way to treat this type of injury. It has the advantage of being less traumatic, enables exclusion of other peritoneal injuries, is cosmetically acceptable, and reduces both length of hospital stay and infection risk.

### References


Complications of Central Venous Catheterisation
Breakage of guidewire—a disaster averted

Qutaiba A. Tawfic, Pradipta Bhakta, *Jyoti Burad, Pragyanidpta Mishra, Rajini Kausalya

CASE REPORT

Patients with sickle cell disease (SCD) often experience degradation of their peripheral veins due to frequent hospital admissions for management of crises and the need for multiple central venous catheter insertion in the later part of their life. The standard Seldinger’s technique for central venous catheter insertion is quick, simple and safe. More than 5 million central venous catheter insertions are performed yearly in the USA alone by physicians and nurses with different levels of experience yet the mechanical complication rate is below 10%. Seldinger’s technique uses a J-tip guidewire for insertion of the central venous catheter; the rare mechanical complications are looping, entrapment or disengagement of venous devices, breakage, embolism, cardiac perforation, tamponade and death. We report such a mechanical complication in a SCD patient with special mention of the anticipated difficulties of central venous catheter insertion in patients who need multiple central venous cannulation.

Case Report

A thirty-one year-old female patient with SCD was admitted to the Intensive Care Unit at Sultan Qaboos University Hospital, Oman, with acute chest syndrome, shock and respiratory distress requiring mechanical ventilation. She was prepared for central venous catheter insertion following failures to obtain good peripheral access. There were several marks and scar tissue on both sides of her neck and upper chest indicating multiple previous central venous catheter insertions.

The pre-procedure ultrasound revealed a good calibre right internal jugular vein in the upper neck, which became slight narrower when traced to the lower angle of Sedillot’s triangle; it had an irregular outline with multiple collaterals. The picture was almost same on left side. The right internal jugular vein was selected for insertions of a 7.0 French triple-lumen central venous catheter using Seldinger’s technique. After obtaining a good back-
Complications of Central Venous Catheterisation

Breakage of guidewire—a disaster averted

flow of blood from an 18-Gauge introducer needle, a J-tip guidewire was advanced. The guidewire encountered mild resistance during insertion, which was overcome by manipulating and redirecting it. The introducer needle was removed and the skin dilator was passed over the guidewire after a small skin nick. There was significant resistance to the advancement of the dilator in the subcutaneous tissue. The skin incision was deepened and the tract was re-dilated with continuous firm pressure on the dilator. After successful dilatation, the central venous catheter was threaded over the guidewire with some resistance; a backflow of blood could be seen in the proximal two lumens confirming the correct position.

While withdrawing the guidewire through the distal lumen, some resistance was encountered. Gentle traction was of no avail; therefore, we advanced the guidewire for a few centimetres to release it from the central venous catheter. The guidewire was rotated by 90 degrees before its withdrawal was again attempted. This time, the guidewire could be retracted few centimetres more. Again, some resistance was encountered; then, there was a sudden loss of resistance after which the guidewire came out.

After removal, we noticed that the J-tip portion was missing. Since we could not trace the J-tip, we removed the entire catheter. Fortunately, the J-tip was inside the catheter half protruding from the tip. Examination of the rest of the guidewire did not reveal any defect other than a sharp bend in the middle [Figure 1]. Later, chest fluoroscopy ruled out the possibility that any broken part of the guidewire had been left inside the patient.

Discussion

Repeated central venous catheter insertion in patients with SCD or those undergoing chemotherapy may have many undesirable consequences. They are at higher risk of thrombosis due to the primary disease and multiple venipuncture attempts, which may later lead to central vein stenosis.6

Stenosis of a vein at higher level in the neck can be diagnosed easily by pre-procedure ultrasound, but lower level stenosis may falsely dilate the internal jugular vein (IJV) in the neck luring the physicians to attempt forceful central venous catheter insertion. It will be difficult or impossible to insert the guidewire/central venous catheter depending on the degree of stenosis. Even after successful central venous catheter insertion, the risk of further stenosis and complete occlusion remains high. There is also a theoretical risk of cannulating the dilated ayzygos and hemiazygos veins if the stenosis is below their union with superior vena cava. This is difficult to diagnose in a chest radiograph unless a lateral view is done where it is seen as acute posterior angulation of central venous catheter tip.7 Scars due to central venous catheter and mediport insertion may cause extensive fibrosis of the skin and subcutaneous tissue and may distort the vascular anatomy. It may pose significant problems when advancing the introducer needle, dilating the guidewire tract and also threading the central venous catheter over the guidewire.7

Ultrasound can be of great help in making a differential diagnosis in this type of patient with multiple previous attempts and anatomical abnormalities. Also ultrasound helps during the procedure in guiding the introducer needle for venous puncture as well as inserting the guidewire in such problematic patients. Even cine-ultrasound can be used to monitor the whole procedure in case a C-Arm is not available. Without ultrasound guidance, carotid artery puncture is very common in these patients due to their distorted anatomy.9 It is difficult to judge how much force is optimum when dilating the tract and excessive force may kink or weaken the guidewire and potentially may puncture or shear the posterior wall of the vein. Therefore, even a good calibre vein seen in pre-procedure ultrasound does not guarantee an easy and successful cannulation in these patients.

Most physicians use the standard J-tip guidewire for central venous catheter insertion. This consists of a stainless steel core wound by a spring. Increased flexibility of the J-tip is obtained at the expense of potential weakness at the junction of the J-tip.4 There are incidental reports of breaking of the J-tip of guidewire during forcible extraction.3,7 Shimamoto and Arai described this as follows: “The guidewire was acutely bent between the first rib and clavicle as a plastic catheter over a needle was used to access the subclavian vein and the guidewire was introduced through the plastic catheter after removing the metal needle.” Lack of experience, improper technique and manufacturing defects have also been cited as the other causes of
breakage. An improved guidewire design has even been recommended by few proponents in order to prevent such a complication.

An experienced resident performed the central venous catheter insertion in our case and no manufacturing defect was found in the guidewire. We believe that difficult anatomy and improper technique were the main factors for the complication in our patient. Stenosis in the vein might have caused an acute angulation of the guidewire. Fibrotic tissue in the neck required excessive force for dilation that kinked and damaged the angulated guidewire. It became lodged in the central venous catheter during removal and broke off at the damaged point in spite of the application of only gentle force.

Thus it is always advisable to use some sort of imaging guidance like ultrasound or fluoroscopy during the whole procedure in problematic cases like this. Even ultrasound can be placed along the long axis of vein and dilator in case of difficult scarred tissue dilatation, as in our case, in order to keep the dilator and the lumen of the vein in view. Also, fluoroscopy should be used in conjunction with this to re-confirm the safety. If the guidewire gets lodged or damaged, the CVC and the guidewire should be removed completely and checked for integrity, but this technique entails re-puncturing the vein. To prevent this, the guidewire should be pushed a few centimetres to dislodge it from the sharp bevel of the introducer needle and then rotated by 90 to 180 degrees. This will straighten the J-tip against the tempered side of introducer needle without damaging it. With this manoeuvre, the guidewire can be withdrawn without disturbing the position of the introducer needle thus preventing re-puncturing the vein.

**Conclusion**

This case reminds of possible anatomical and iatrogenic venous deformities in patients requiring multiple central venous cannulations, such as patients with SCD or on chemotherapy. These can result in disastrous complications during CVC insertion if there is forcible dilatation of the scarred subcutaneous tissue. Routine use of ultrasound and fluoroscope guidance throughout the procedure can be of great help in avoiding such complications.

**References**

A 62-year-old woman, diagnosed with and on treatment for hypertension, was referred to the Haematology Department at the Royal Hospital, Oman, with an accidental finding of increased white blood cells (WBC) in her full blood count, a total of 76 x 10^9/L. There was history of giddiness, fever and easy fatigability prior to presentation.

A repeat blood work-up showed a haemoglobin level of 10.8 g/dl, with normal mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH), a platelet count of 55 x 10^9/L and a WBC count of 103 x 10^9/L. All other blood investigations including renal function tests, liver function tests and bone profile, were normal. Viral studies, blood and urine cultures were negative. The blood film showed >90% large sized blasts with abundant cytoplasm and prominent nucleoli [Figure 1A]. The bone marrow aspirate (BMA) [Figure 1B] and flow cytometry findings were consistent with acute myeloid leukaemia (AML-M1) according to the French-American-British [FAB] classification. Later, cytogenetic investigation revealed a positive FLT-3 mutation.

On the second day of admission, she was found to have a neck swelling and developed shortness of breath. An emergency neck computed tomography (CT) scan was done [Figure 1C] which showed a soft tissue thickening (mass) of the nasopharynx and oropharynx encroaching on the airway and almost occluding it. The patient was started on standard induction chemotherapy, (cytarabine once daily for seven days and daunorubicin twice daily for three days intravenously), as well as prophylaxis with antiviral and antifungal medications.

The patient remained stable and afebrile. She was discharged 22 days after the induction of chemotherapy, with a haemoglobin level of 9.6 g/dl and platelet count of 44 x 10^9/L. A week later she was seen in the day care unit, had a
repeat blood film and BMA done which was consistent with morphologic remission [Figure 2 A & B]. A repeat neck CT scan showed that the previously noted soft tissue thickening in the nasopharynx and oropharynx had disappeared as well [Figure 2C]. A biopsy of the mass was not done earlier due to the location and the high risk of bleeding in this case. However, it disappeared after treatment and this would indicate that it was a leukaemic tissue mass. She received two consolidation chemotherapies followed by allogenic bone marrow transplantation. However, she relapsed after three months and died.

The main presentations in patients with AML include peripheral blood and bone marrow involvement. Extramedullary presentations, such as head and neck swellings, have been reported. In our literature search, we found only a few cases with some resemblance to ours. De Fonseca reported a child with a neck swelling who sought medical attention from a dentist where no odontogenic problem was found; however, he was subsequently diagnosed to have AML.1 Hayashida et al. described a nasopharyngeal mass in a patient diagnosed with acute monocytic leukemia.2 Udayakumar and Sundareshan reported a girl with neck swelling who was diagnosed with AML-M6.3 Amin et al. mentioned that AML subtypes M4 and M5 have a higher incidence of oral infiltrations and reported one case of AML-M0 which presented with palatal swelling.4 An AML case, occurring in the tonsillar fossa as an ulcerating lesion with a neck mass, has also been described.5 A patient who achieved remission following the diagnosis of an AML-M0, presented with a mass in the left retropharyngeal and perivertebral regions, a mass in the left vallecula, and a mass infiltrating the right preepiglottic tissue. He was later diagnosed to have granulocytic sarcoma.6 Finally, another study was conducted to summarise the clinical and radiologic presentations including pertinent imaging features of granulocytic sarcoma. The lesions were mainly found in the central nervous system, subcutaneous tissues, and genitourinary system.7 No articles were found in the literature mentioning an AML-M1 case with neck swelling or nasopharynx involvement.

References

Is it not the time to stop the use of Scoline® (suxamethonium chloride) for rapid sequence intubation?

Sir,

In 1992, the USA Food and Drug Administration (FDA) issued a warning in the Scoline® (suxamethonium chloride, GlaxoSmithKline, USA) package insert after receiving reports of intractable cardiac arrests. It stated: “Since there may be no signs or symptoms to alert the practitioner as to which patients are at risk, it is recommended that the use of succinylcholine in children should be reserved for emergency intubation or instances where immediate securing of the airway is necessary, e.g. laryngospasm, difficult airway, full stomach or intramuscular (IM) use when a suitable vein is inaccessible.”

Scoline® has been used for rapid sequence tracheal intubation since its introduction into clinical practice in Europe in 1951 and in the USA in 1952. It gained popularity for its quick onset (less than 60 seconds) and ultrashort duration of action. Scoline® came to rule the practice of anaesthesia and continues to do so even today. It is the gold standard against which the other muscle relaxants are compared; however, a number of clinical case reports have shown clearly that the use of scoline has been associated with a number of serious adverse effects and its use has declined since 1992.

In our hospital, there have been cases (unpublished reports) of prolonged apnoea and trismus following scoline use. Since it is not possible to predict at the outset which patient will have prolonged apnoea unless a family history is available, is it prudent to use scoline in cases of anticipated difficult intubation? Cardiac arrests after Scoline® use have been reported in Japan in pregnant patients who had been immobilised due to concern about preterm labour. A couple of reports even mention that the use of Scoline® led to a ‘can’t ventilate and can’t intubate’ situation due to severe trismus in an emergency and even following attempts at routine intubation. Are these adverse effects acceptable in current day practice of medicine and anaesthesia?

For the quick onset of relaxation of vocal cords, rocuronium bromide, a non-depolarising muscle relaxant, is available (Esmeron® N.V. Organon, Oss, Netherlands). It was introduced in clinical practice in 1994 and has been used in many countries for the last 17 years. It belongs to the aminosteroid group and studies show that it achieves rapid onset of good intubating conditions within 60 seconds if a dose of 1.2 mg /kg is given intravenously. In patients for whom intravenous access is not available it can even be administered intramuscularly. It has been safely administered in the paediatric age group from 1–24 months of age.

When comparing the intubating conditions between rocuronium and Scoline®, the Cochrane database meta-analysis found that rocuronium is less effective than succinylcholine for creating excellent intubation conditions and recommended that rocuronium should therefore only be used as an alternative to succinylcholine when it is known that succinylcholine should not be used. However, in an emergency situation it is not known and cannot be predicted which patient will have an adverse reaction to Scoline®.

On reviewing and comparing the overall safety and efficacy profile, rocuronium has not shown any of the serious adverse reactions seen with scoline. It is even used safely in asthmatic patients. The only adverse reaction is hypersensitivity, but the overall incidence is not more than Scoline®, or other non-depolarising muscle relaxants. The main concern with rocuronium has been the long duration of action. The possibility of awakening the patients in case of an inability to ventilate was the main reason preventing the use of this drug for rapid sequence intubation.

With the availability of sugammadex sodium (Bridion®, Schering-Plough Merck, USA) this should no longer be a barrier to using rocuronium. It has been recommended to the cardiac anaesthesiologist for clinical use for high risk patients at appropriate doses. Sugammadex is a cyclodextrin derivative which seems to
provide a faster onset-offset profile than that seen with 1.0 mg/kg succinylcholine. This drug has even been used as an antidote to the muscle relaxant in case of a hypersensitivity reaction. It was approved for clinical use by the European Medicines Agency in 2008. It awaits FDA approval in the USA due to concerns about its hypersensitivity, but there is no concern about its efficacy.

Nowadays, we have intubating laryngeal mask airway (ILMA), proseal airway and gum elastic bougie for securing the airway in case intubation is difficult. We would not like any patient to develop severe trismus and make the possibility of ventilating difficult or even impossible in an emergency situation.

Therefore the time has now come to reconsider the recommendations and indeed to discontinue the use of Scoline® for rapid sequence intubation.

CONFLICT OF INTEREST

The author has declared no conflict of interest and is in no way influenced by the manufacturers of any drug mentioned in this letter.

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References

Is it not the time to stop the use of Scoline® (suxamethonium chloride) for rapid sequence intubation?


Sir,

Recurrent laryngeal nerve (RLN) paralysis is a devastating complication after thyroid surgery. Although the incidence has decreased from 17% to as low as 1.5% with evolution of surgical technique, it still remains high in cases involving re-exploration, malignancy, radiation exposure, and large goitres.1 Some of the important causes of RLN injury during thyroid surgery are application of excessive stretch, pressure, suction, electrocautery and ischaemia which may go unnoticed during surgery. Symptoms of RLN palsy are dysphonia, dysphagia, aspiration, voice alteration and life threatening dyspnoea from airway obstruction.1,2 Thus, although the incidence of permanent paresis of the RLN after thyroidectomy is low, it can have serious consequences and is of significant medicolegal importance. It is therefore vitally important that during the perioperative period both the anaesthesiologist and the surgeon assess the vocal cord function (VCF) of a patient undergoing thyroidectomy.

Preoperative indirect laryngoscopy by an otolaryngologist is a simple examination to know the base line VCF.3 Similarly, intraoperative neuromonitoring (IONM) is used to localise the RLN and prevent impending RLN injury during the surgical instrumentation.4 Finally, direct laryngoscopy after tracheal extubation can assess the VCF immediately after surgery and rule out the risk of acute airway compromise.3

There is no uniform opinion about the constant question whether laryngoscopy at the end of thyroid surgery is an essential standard or just an unnecessary routine. The answer might depend on the specific hospital protocol and the presence of factors related to the gland itself which increase the risk of RLN injury.3 Our hospital is a tertiary care referral center and we regularly do difficult thyroid surgeries which include malignancy, big thyroid with retrosternal extension; we also redo thyroidectomy for recurrent nodule or goitre. Assessment of VCF is routinely done after these surgeries and our surgeons expect to be provided with the results.

The GlideScope®, which has recently become a very important piece of equipment in the anaesthesiologist’s armamentarium, is a videolaryngoscope. This has a digital camera incorporated into the blade which displays a view of the vocal cords (VCs) on a monitor.5 Recently, we have started using a GlideScope® to look at the post-extubation VCF after thyroid surgery and found it very advantageous. Its exaggerated blade curvature and camera with enhanced optics placed at the inflection point of the blade gives a better magnified view with a larger viewing angle of the glottis even without the proper alignment of the oral and tracheal axis. Therefore, the GlideScope®, compared to a conventional laryngoscope, requires less forceful displacement of the tongue and less forceful manipulation of the larynx while attempting to view the VCs.5,6

The above features make the GlideScope® much more suitable for proper assessment of post-operative VCF when the patient is recovering from the neuromuscular blocker and general anaesthetics and can resist the use of airway instrumentation. A reduced amount of airway manipulation will have lesser systemic side effects such as hypertension, tachycardia, cough, laryngospasm, increased intra-cranial and intra-ocular pressure. Similarly, the risk of disruption to skin sutures in the neck, or bleeding due to laryngeal
manipulation will also be reduced.\textsuperscript{5}

In addition to patient safety, the GlideScope\textsuperscript{®} provides clearer visualisation of the VCs compared to a conventional laryngoscope. Its video screen can be shared with other physicians in the operating theatre including the surgeon.\textsuperscript{6} In addition to confirming the VCF with the surgeon, capturing a video of VC movement can be very useful for documentation purposes. Also, in the case of any VCF abnormality, it can be treated as a baseline evaluation for future follow-ups. In patients with established difficult airway, the GlideScope\textsuperscript{®} may be the only way to visualise the VCs during intubation and after extubation if a fibreoptic bronchoscope is not available.\textsuperscript{5,7}

In summary, although further randomised clinical trials are required, the GlideScope\textsuperscript{®} looks to be a better and safer choice for assessment of post-extubation vocal cord function after thyroid surgery compared to a conventional laryngoscope.

CONFLICT OF INTEREST

The authors reported no conflict of interest and are in no way influenced by the manufacturers of any equipment mentioned in this letter.

References


Sir,

I read with interest the published article by Al-Shamahy et al. in your journal. It is an important report which encourages health policy makers to control hepatitis B virus (HBV) infections more effectively. I would like to add some information which may improve the understanding of the situation. HBV is a common cause of liver disease in the world and most of the sufferers are Asians. Universal vaccination in Iran since 1993 of all neonates against hepatitis B virus has changed the epidemiology of this infection. Similar experiences have been reported from other countries such as Saudi Arabia and China. Improvement of people’s knowledge about HBV risk factors, national vaccination programmes for all neonates, vaccination of high risk groups, such as health care workers, and the introduction of disposable syringes for use in vaccinations, hospitals and clinics might explain this decrease.

It is important for a country such as Yemen with HBsAg positivity of more than 6% in pregnant women, to formulate a better policy for the control of HBV infection. The age at which HBV infection occurs influences the rate of transmission, the long-term outcome and determines the primary targets of a vaccination programme. Thus, perinatal transmission from mother to child occurs soon after birth results in about 90% chronic carriage, with its long-term complications of chronic hepatitis, cirrhosis and hepatocellular carcinoma, leading to death in middle age. This has serious economic consequences for the family and for the country as a whole. The contribution of each mode of transmission to morbidity and mortality must be known in order to develop the optimal vaccination programme.

The authors excluded the anti-HBcAb positive subjects from the vaccinated group in order to differentiate them from those with naturally occurring to HBV infection. However, as we have reported before about the outcome after HBV vaccination in infants of HBsAg mothers, 23% of these infants were anti HBcAb positive. This means that the HBV vaccine prevented HBV infection.

The authors recommend that children who were non-responders to HBV vaccine be re-vaccinated, but I think the first strategy should be to focus on increasing the coverage of HBV vaccination in infants. The World Health Organization (WHO) recommended that all countries which have reached a satisfactory coverage level of hepatitis B immunisation through routine vaccination develop other strategies for the control of HBV infection in their community.

Finally, I would like to mention that HBV vaccine is a temperature-sensitive biological product and exposure to heat shortens its shelf life, while freezing causes irreversible loss of potency. I therefore recommend the evaluation of an outside-the-cold-chain vaccine delivery system in Yemen. I hope for better prospects for HBV infection control in the future in our region.

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Re: Hepatitis B Vaccine Coverage and the Immune Response in Children under ten years old in Sana’a, Yemen—We need to work much harder to control hepatitis B virus infection in developing countries

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References


Author's Response

Dr. Alavian's careful reading of our article and his subsequent comments are acceptable. He raises several points and we would like to respond to each of them.

First, Dr. Alavian added some information which may improve the understanding of the situation and change the epidemiology of this infection by improvement of people's knowledge about HBV risk factors. National vaccination programmes for all neonates, vaccination of high risk groups such as health care workers and the introduction of disposable syringes for use in vaccinations, hospitals and clinics might explain the decrease in HBV rates in some countries.1 I agree with him, but often there are many obstacles which suddenly rise up like the situation now in Yemen where the national vaccination programme is stopped due to what is called a revolution (civil war). Also I agree with his second point as a high rate of liver cancer in Yemen is now occurring in individuals in their early forties.2 The third point was why we excluded the anti-HBcAb positive subjects from the vaccinated group in order to differentiate them from those with naturally occurring HBV infection. We did this because the anti-HBsAg might be due to natural infection and not due to vaccine.3 The fourth point was where we recommended that children who were non-responders to HBV vaccine be re-vaccinated; in addition, we have also recommended increasing the coverage of HBV vaccination in infants. However, just increasing the vaccination coverage may still lead to a high rate of failure because of non-response rates.

Finally, we agree with him about the effect of temperature on the failure of the vaccine as HBV vaccine is a temperature-sensitive biological product and exposure to heat shortens its shelf-life, while freezing causes irreversible loss of potency. Thus we agree with his recommendation of the evaluation of an outside-the-cold-chain vaccine delivery system in Yemen.

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Sir,

We compliment Al-Araimi and colleagues for recommending prospective awareness for medical personnel about different travel-related tropical diseases including dengue fever.¹

Their 38 year-old Sri Lankan patient¹ tested negative with polymerase chain reaction giving an equivocal result for Dengue IgM. Serum sample(s) collected after two or more months should be tested for Dengue IgG. In all probability, the levels of IgM and dengue virus ribonucleic acid had reached undetectable levels. The demonstration of dengue virus IgG would reconfirm the initial diagnosis.¹

In countries known to be free of dengue virus infection, travel-related importation would be a problem for clinicians and laboratory personnel. A point-of-care assay for dengue virus non-structural protein1 (NS1) antigen, anti-dengue IgM and IgG would be very practical. During the initial phase of illness, NS1 would be the earliest datable marker in any primary or secondary infection. That would be followed by an appearance of IgM in a primary infection or IgG in a secondary infection.

The results of the 23 dengue-virus positive cases detected at the Narita Airport Quarantine Station, Japan are of interest in this regard.² There was almost identical sensitivity of the dengue virus (DENV) NS1 antigen detection by the ELISA and the rapid test. The IgM/IgG detection, employing either the antibody-capture ELISA or the rapid test, was not found to be suitable to identify any DENV-carrying individuals arriving in countries reported to be dengue free.

The utility of a single-step immunochromatographic one step dengue NS1 Ag and IgG/IgM test, (Dengue Duo; Standard Diagnostics, Inc, St. Ingbert, Germany: www.standard.com) was immense during the 2010 DENV outbreak in Delhi, India. Among 175 suspected cases, 86 were NS1 positive and 89 were NS1 negative. Among 86 NS1-positive patients, 23 were IgM positive, four were IgG positive and six were positive for all three markers. The 89 NS1-negative patients included two who were IgM positive, eight who were IgG positive and seven who were positive for both IgM and IgG: 72 were negative for all three markers and 53 patients were positive exclusively for NS1. Using the Dengue Duo test, it was possible to diagnose 61 additional patients: these NS1 positives included 57 who were negative for IgM and four who were positive for IgG only.³

To conclude, awareness among medical and health care personnel in dengue free countries¹ as well rapid disease diagnosis would ensure better clinical management and public health response to halt any local dengue transmission.

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References

Globally, obesity has now reached epidemic proportions. Although the prevalence is highest in developed countries, obesity has become an important health issue in many developing countries, often co-existing with undernutrition.

Concomitant with the increased rates of obesity in the general population, rates during pregnancy have also escalated, and obesity is now a common high-risk obstetric condition. Information is limited on the prevalence of overweight and obesity during pregnancy in various countries. According to this book, the reported prevalence of maternal obesity in different cities and states of the USA ranged from 10% to 26%.

Obesity is not only a health issue, but also has economic consequences. Total costs involve both direct costs related to medical expenditure on obesity-related diseases (including type 2 diabetes, cardiovascular diseases, several types of cancers and musculoskeletal disorders) as well as indirect costs related to absenteeism, reduced productivity, and disability. Studies from many countries have reported on the substantial and increased economic burden of obesity. Recognition of this problem has led to an explosion of research into causes and solutions, from the genetic to the population level and all points in between.

The pregnancy care of obese and overweight women provides a unique set of challenges. Excess weight affects fertility, pregnancy, delivery and the postpartum period. A specialised knowledge base and skill set are required to provide competent pre-pregnancy, obstetric and postnatal care to obese women. The aim of this book is to supply this knowledge to busy clinicians facing just such challenges. The reader will find collected in one location information covering every aspect of pregnancy in obese women beginning with the epidemiological scope of the problem and ending with postpartum care. This is the first edition of the book, edited by Deborah L. Conway of the
There is a growing body of evidence to suggest that obese women experience more psychological stressors and psychological disorders than normal weight women. In this book, composed of 14 chapters, the second one describes the psychological aspects of obesity in women outside of and during pregnancy and offers pragmatic screening tools for use in clinical assessment during pregnancy.

In addition to the typical obstetrics topics like prenatal care, fetal surveillance and delivery, in chapter 4 the book addresses bariatric surgery (vertical banded gastroplasty and Roux-en-Y gastric bypass). This surgery is recommended for women with a body mass index of 40 kg/m² or over who have failed at conventional weight loss attempts, have been properly educated and are motivated for surgery. Chapter 5 deals with post-bariatric surgery pregnancy-related complications like hypertensive disorders and gestational diabetes. Caesarean sections are more prevalent in women who have undergone bariatric surgery. However, there is no difference between them and the general population in intra-partum complications like placental abruption, labour dystocia and meconium-stained amniotic fluid. Chapter 5 also covers fetal malformation and birth weight problems like small for gestational age neonates and macrosomia.

The reader will find covered in this book the special considerations needed in prenatal care for obese women and the limitations of ultrasound in anomaly detection as well the difficulty of invasive testing. It also covers late pregnancy and intra-partum care, especially breech presentation and trial of labour in obese women.

Other chapters address the adverse consequences of maternal obesity during pregnancy, as well the adverse effects on child health outcomes later in life such as: child, adolescent and adult obesity; high blood pressure; metabolic syndrome, and cardio-metabolic complications. Chapter 13 focuses on the preparation of the obese pregnant women for surgery and anaesthetic considerations as well antibiotics and pre-operative and post-operative care.

The last chapter, the most interesting one in my opinion, focuses on how obesity affects breastfeeding and contraception. The various contraception methods are described in detail. Since obesity increases the failure rates of several methods, the book proposes that there is a need for in depth evaluation, which should take into consideration the woman’s personal, social, family and medical history.

This book is unique on several scores. It focuses on a problem that has now reached epidemic proportions and uses evidence-based medicine to cover many aspects of obesity in pregnancy in one volume. It is an excellent source of up-to-date information and, in addition, it is very easy to read and digest. Overall, this book is therefore a useful resource for medical students, obstetric residents, and general and high-risk obstetricians.

I will definitely use this book for reference and I highly recommend it to others.

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Overview of Obstructive Sleep Apnoea including Historical Background, Pathophysiology and Clinical Presentations
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Obstructive sleep apnoea (OSA) is a common disorder characterised by repetitive narrowing or collapse of the pharyngeal airway during sleep. Estimates of disease prevalence are in the range of 2% to 4%, with certain subgroups of the population bearing higher risk. The disorder is associated with major co-morbidities including excessive daytime sleepiness and increased risk of cardiovascular disease. The underlying pathophysiology is multifactorial and may vary considerably between individuals. Important risk factors include age, male sex, obesity, family history, menopause, craniofacial abnormalities, and certain health behaviours such as alcohol use. Despite the numerous advancements in our understanding of the pathogenesis and clinical consequences of the disorder, a majority of those affected remain undiagnosed. In this presentation, the historical background of obstructive sleep apnoea will be briefly covered. The current understanding of OSA pathophysiology in adults, the potential mechanisms underlying the principal risk factors and various clinical presentations of this disease will be discussed.

Diagnosis of Obstructive Sleep Apnoea
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Obstructive sleep apnoea (OSA) is a disorder characterised by obstructive apnoeas and hypopnoeas caused by repetitive collapse of the upper airway during sleep. According to American Academy of Sleep Medicine, the Criteria for definition of obstructive apnoea are (all 3): 1) Cessation of air flow; 2) continued respiratory effort, and 3) apnoea lasting 10 seconds or longer. A central apnoea occurs when both airflow and ventilatory efforts are absent. Mixed apnoea occurs when there is an interval during which there are no respiratory efforts and an interval during which there are obstructed respiratory efforts. Diagnosis of OSA is suspected from history and physical examination and confirmed by a sleep study using polysomnography (PSG). Snoring and excessive daytime sleepiness are the most important symptoms. Interestingly, it has been noted that women report symptoms of OSA less frequently. The Epworth Sleepiness scale (ESS), a subjective test, measures sleepiness as it occurs in ordinary life situations. It can be used as a screening test for excessive sleepiness, or to follow an individual's subjective response to an intervention. Physical examination is frequently normal. Obesity and crowded oro-pharynx are the most important findings. Hypertension or uncontrolled hypertension is also a significant observation. The Mallampati score (MS) is an important tool to assess the upper airway; MS 3 and 4 have good sensitivity and specificity. The differential diagnosis of OSA include periodic limb movements of sleep, sleep pattern of rotating shift workers, narcolepsy, upper airway resistance syndrome and simple snoring. For diagnosis, full-night or split-night, attended, in-laboratory polysomnography is suggested for most of the patients. Unattended portable monitoring is an alternative test for patients in whom there is a high likelihood of moderate or severe OSA. The severity of OSA is graded using the Apnoea Hypopnoea Index (AHI) which equals the number of apnoeas and hypopnoeas occurring per hour of sleep. AHI of 5–15 defines mild OSA, 15–30 moderate OSA and AHI > 30 severe OSA.

Complications of Obstructive Sleep Apnoea/Hypopnoea Syndrome
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The obstructive sleep apnoea/hypopnoea syndrome (OSAHS) is a common disorder, affecting around 2–4% of the middle-aged population. There is a strong association between OSAHS and hypertension, ischaemic heart diseases stroke and type 2 diabetes. Different mechanisms play a role in the process of developing complications in OSAHS.
Obstructive sleep apnoea (OSA) is a common under diagnosed disorder characterised by recurrent upper airway obstruction during sleep. The prevalence of OSA is estimated to be around 4% in middle aged men and 2% in females in the same age group. In addition to its numerous medical consequences, OSA has its own effects on the psychosocial well being of the affected individuals and can adversely impact health care economics. Daytime sleepiness, one of the main symptoms of OSA, adversely affects cognition which impairs the work performance. It can also result in deficits in neurocognitive performance which in turn leads to errors while driving and result in increased risks of motor vehicle crashes, including a high rate of collisions in patients who drive as part of their occupation. In one of the studies, the risk of occupational accidents was found to be 50% higher in those with OSA compared to normal controls. OSA appears to cause a huge economic burden. The economic burden of OSA-related automobile collisions alone is enormous. To illustrate this, patients with sleep apnoea have a three to seven fold increased risk of motor vehicle crashes and CPAP reduces these risks substantially; Sassani et al. reported that in the year 2000 there were 810,000 collisions and 1,400 fatalities attributable to OSA in the USA with a total cost of 15.9 billion dollars. Treatment with CPAP would have prevented 567,000 of these crashes, saved approximately 1,000 lives, and resulted in an overall savings of 7.9 billion dollars after costs associated with treatment were taken into account. Untreated OSA leads to multiple medical problems (such as systemic hypertension, cardiovascular disease, injuries and mood disorders) that increase health care utilisation. Patients with sleep apnoea can consume 1.7 times more health care resources than controls matched for age, gender, area of residency and family physician. The total economic burden of sleep disorders in Australia (a country with a population of 20.1 million) was substantial: $7.494 billion in 2004. The financial costs, excluding the cost of suffering, were $4.524 billion, representing 0.8% of Australia’s gross domestic product. CPAP therapy for OSA appears to reduce health care utilisation. More importantly, it is cost effective—more so than fluticasone for asthma and primary angioplasty after myocardial infarction as assessed by the incremental cost-effectiveness ratio (ICER), which is the ratio of the incremental cost and incremental change in quality-adjusted life years (QALY) that follows from the adoption of a treatment (CPAP in case of OSA).

### Medical Treatment of Obstructive Sleep Apnoea

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Obstructive sleep apnoea is a disease characterised by obstructive apnoeas and hypopnoeas due to upper airway collapse. Medical therapy involves mainly the use of continuous positive airway pressure (CPAP) devices that basically work by blowing air into the upper airways under constant pressure to prevent or correct the collapse of the airways during sleep. There is high quality evidence that CPAP therapy improves daytime sleepiness, cognitive function and quality of life. Treatment also improves the cardiovascular consequences of OSA. CPAP machines either deliver a constant pressure throughout the night (fixed CPAP), or variable pressure depending on a specific algorithm (auto CPAP). There is no consensus on the optimal duration for using CPAP, but use for more than five hours every night is preferred. Compliance with CPAP therapy remains an issue with most patients having poor adherence. This might be improved with proper patient counselling and trial of various forms of masks that will fit the particular patient best. Medical therapy in terms of using pharmacological agents has not been shown to be effective; however, it can be used as an adjunctive therapy in patients who continue to have daytime sleepiness despite proper and adequate use of CPAP.

### Role of Oral and Maxillofacial Surgery in the Management of Obstructive Sleep Apnoea

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Oral and maxillofacial surgery plays an important role in the management of patients with sleep apnoea. The oral and maxillofacial surgeon can screen the patients in the outpatient clinic, manage associated orofacial symptoms (bruxism, temporo mandibular disorders, etc), provide mandibular advancement devices and offer maxillofacial surgeries to improve the airflow at the oropharynx area. Usually patients are referred to the maxillofacial surgeon after the diagnosis and severity of their apnoea are established by a sleep study. In addition, endoscopic airway assessment by an ENT specialist can be performed to identify the site of obstruction and which surgical procedures would be most effective in improving airflow.
decreased respiratory rate, increased tidal volume and a good patient-ventilator synchrony. Oxygen is supplemented as of 2 cm H2O or as tolerated (IPAP 20-25 and EPAP 10-15 cm H2O maximum) to achieve alleviation of dyspnoea, with care to minimise excess pressure on the face or nose. The pressures can then be gradually increased in increments place by the therapist to familiarise the patient with the flow. Then the straps should be applied to hold the mask in place, mode with backup rate, applying 8 to 12 cm H2O of IPAP and 3 to 5 cm H2O of EPAP. The mask should be first held in provides flow and volume assistance with each breath. It is better to start with low pressure in spontaneously triggered (IPAP) and expiratory positive airway pressure (EPAP) separately. Another mode, proportional-assist ventilation (PAV) (BPAP) is probably the most common mode of support and requires provision of inspiratory positive airway pressure with advancement genioplasty or even tracheostomy may be indicated. In OSA, the success of surgery is generally measured by achieving a respiratory disturbance index (RDI) of less than 5, improvement of oxygen saturation to 90 per cent or more and quality of life improvements with elimination or significant reduction of OSA symptoms. It is extremely difficult in practice to achieve these goals without the cooperation of the patient, especially weight loss and maintenance of a healthy lifestyle. Finally, continuous positive airway pressure (CPAP) is the gold standard treatment for OSA, surgical management only being an adjuvant.

Surgical Approach for Obstructive Sleep Apnoea
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Obstructive sleep apnoea (OSA) syndrome is a potentially serious disorder affecting millions of people around the world. It involves periodic partial or total collapse of the pharyngeal airway during sleep. This results in progressive asphyxia, which increasingly stimulates breathing efforts against the collapsed airway, typically until the patient is awakened from sleep. The intention of surgery in OSA is to open the airway sufficiently to eliminate or to reduce obstructions to a clinically insignificant level. The most commonly performed procedures include nasal reconstruction, adenotonsillectomy, uvulopalatopharyngoplasty (UPPP), advancement genioplasty, mandibular osteotomy with geniohypothesis advancement, and hyoid myotomy and suspension. In more severe cases, maxillomandibular advancement (MMA) with advancement genioplasty or even tracheostomy may be indicated. In OSA, the success of surgery is generally measured by achieving a respiratory disturbance index (RDI) of less than 5, improvement of oxygen saturation to 90 per cent or more and quality of life improvements with elimination or significant reduction of OSA symptoms. It is extremely difficult in practice to achieve these goals without the cooperation of the patient, especially weight loss and maintenance of a healthy lifestyle. Finally, continuous positive airway pressure (CPAP) is the gold standard treatment for OSA, surgical management only being an adjuvant.

Insomnia, Assessment and Treatment
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Insomnia is the most prevalent sleep disorder in the general population and is commonly encountered in medical practices. Its prevalence is estimated to be around 20%. Insomnia is defined as a subjective perception of difficulty with sleep initiation, duration, consolidation, or quality that occurs despite adequate opportunity for sleep leading to some form of daytime impairment. Insomnia may present with a variety of specific complaints and aetiologies, making the evaluation and management of this disorder demanding on a clinician’s time. In this presentation, the epidemiology, risk factors, pathophysiology, and consequences of insomnia will be briefly discussed. The different types of insomnia, its evaluation and available effective treatments will also be highlighted.

Non-Invasive Ventilation: Practical aspects
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Noninvasive ventilation (NIV) is a form of assisted ventilation without an invasive artificial airway. It is now increasingly used in the first line management of both acute and chronic respiratory failure in the hospital as well as in the home setting. Ventilation is delivered through a noninvasive interface like a nasal mask, facemask, total face mask or nasal pillows. The key to the successful application of noninvasive ventilation is in recognising its capabilities and limitations. Patients who require immediate intubation should not be offered NIV. Relative contraindications include cardiac or respiratory arrest, inability to cooperate, inability to protect the airway or clear secretions, severely impaired level of consciousness, facial surgery, trauma or deformity, high risk for aspiration and recent oesophageal anastomosis. Many patients are provided with the most basic level of support, the continuous positive airway pressure (CPAP). CPAP may be especially useful in patients with pulmonary oedema or obstructive sleep apnoea. Bi-level positive airway pressure (BIPAP) is probably the most common mode of support and requires provision of inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP) separately. Another mode, proportional-assist ventilation (PAV) provides flow and volume assistance with each breath. It is better to start with low pressure in spontaneously triggered mode with backup rate, applying 8 to 12 cm H2O of IPAP and 3 to 5 cm H2O of EPAP. The mask should be first held in place by the therapist to familiarise the patient with the flow. Then the straps should be applied to hold the mask in place, with care to minimise excess pressure on the face or nose. The pressures can then be gradually increased in increments of 2 cm H2O or as tolerated (IPAP 20-25 and EPAP 10-15 cm H2O maximum) to achieve alleviation of dyspnoea, decreased respiratory rate, increased tidal volume and a good patient-ventilator synchrony. Oxygen is supplemented as
Narcolepsy

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Narcolepsy is the second most common cause of disabling daytime sleepiness after sleep apnoea. Descriptions of the disorder appeared as early as 1862. The term narcolepsy was first applied by Gelineau to a clinical syndrome of daytime sleepiness with cataplexy, hypnagogic hallucinations, and sleep paralysis. The prevalence of narcolepsy with cataplexy is estimated to be 25–50 cases per 100,000. It is equally common in both genders. It typically begins in the teens and early twenties, but can occur as early as five years of age or after 40 years of age. The symptoms may worsen during the first few years and then persist for life. Narcolepsy is a disorder of sleep-wake state control in which elements of sleep intrude into wakefulness and vice versa. Only about one third of the affected patients will have the four classic symptoms of daytime sleepiness, hypnagogic hallucinations, sleep paralysis, and cataplexy. Thus diagnosis of narcolepsy should be considered even in patients with sleepiness alone. Patients with untreated narcolepsy typically have Epworth Sleepiness Scale (ESS) scores greater than 15. Loss of orexin signalling, genetic factors, and rare brain lesions can cause or contribute to narcolepsy. Diagnostic testing for narcolepsy includes an overnight polysomnogram (PSG) followed by a Multiple Sleep Latency Test (MSLT). The PSG evaluates sleep quality and can identify coexisting causes of sleepiness such as obstructive sleep apnoea, periodic limb movements of sleep, or REM behaviour disorder that are common in narcolepsy and may warrant specific treatment. MSLT is performed the day after the PSG. During the MSLT, the patient is given four or five opportunities to nap every two hours. On average, healthy subjects fall asleep in about 10 to 15 minutes, whereas people with narcolepsy often fall asleep in less than five minutes, providing objective evidence of their

Sleep from an Islamic Perspective

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Sleep medicine is a relatively new scientific specialty. Sleep is an important topic in Islamic literature, and the Quran and Hadith discuss types of sleep, the importance of sleep, and good sleep practices. Islam considers sleep as one of the signs of the greatness of Allah (God) and encourages followers to explore this important sign. The Quran describes different types of sleep, and these correspond with sleep stages identified by modern science. The Quran discusses the beneficial effects of sleep and emphasises the importance of maintaining a pattern of light and darkness. A mid-day nap is an important practice for Muslims, and the Prophet Muhammad peace be upon him (pbuh) promoted naps as beneficial. In accordance with the practice and instructions of Muhammad (pbuh), Muslims have certain sleep habits and these sleep habits correspond to some of the sleep hygiene rules identified by modern science. Details of how to sleep include sleep position—like encouraging sleep on the right side and discouraging sleep in the prone position. Dream interpretation is an established science in the Islamic literature and Islamic scholars have made significant contributions to the theories of dream interpretation. We suggest that sleep scientists examine religious literature in general, and Islamic literature in particular, to understand the views, behaviours, and practices of ancient people about sleep and sleep disorders. Such studies may help to answer some unresolved questions in sleep science or lead to new areas of inquiry.

Restless Leg Syndrome and Periodic Limb Movement

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Restless leg syndrome (RLS) is a chronic neurological disorder which is underreported; various reported prevalence rates range from 2–15%. Four diagnostic criteria are being identified in order to diagnose RLS, including an urge to move the legs associated with unpleasant sensation in the legs which begin or worsen at rest, in particular at night. The symptoms are relieved partially or completely by movement. It is at times associated with period limb movement (PLM) during sleep. RLS and PLM can lead to significant sleep disturbance and poor quality of life. Both conditions are chronic with 45% of patients experiencing their first symptoms before the age of 20. The frequency and severity of symptoms worsen with time and most of the patients will start feeling their symptoms on daily basis between the ages of 40–60. The pathophysiology is still not well understood, but the dopamine pathway system, brain iron metabolism and endogenous opioids system are being implicated. Most of the time, the aetiology is unknown. However, both RLS and PLM are reported in patients with anaemia, uraemia, and neuropathy. It is important to differentiate RLS and PLM from other conditions like akathisia, nocturnal leg cramps, painful legs and moving toes, peripheral vascular disease and peripheral neuropathy. There are various scales available to assess the severity and quality of life of these patients as well as how to quantify the symptoms in sleep laboratory. Most patients respond well to one of the dopamine agonists. In severe cases, other options may be considered including opioids and antiepileptics.
sleep propensity. The naps of narcoleptics often include REM sleep, and the occurrence of two or more of these sleep-onset REM periods (SOREMs) is an essential feature in establishing the diagnosis of narcolepsy. Narcolepsy without cataplexy can be confirmed if a) chronic sleepiness is accompanied by a MSLT showing an average sleep latency less than eight minutes and/or at least two SOREMs and b) alternative aetiologies have been excluded by history, clinical examination and PSG (e.g., untreated sleep apnoea, periodic limb movements of sleep, insufficient sleep, or sedating medications). Patients with narcolepsy can benefit from a regular and adequate sleep schedule, scheduled daytime naps, avoidance of drugs that produce daytime sleepiness or insomnia, and joining a psychosocial support group. Coexisting sleep disorders need to be treated if present. Patients with sleepiness severe enough to require medication can be treated with stimulant medications, such as modafinil. REM sleep-suppressing drugs which can selectively inhibit the reuptake of norepinephrine or serotonin such as venlafaxine, atomoxetine and fluoxetine may substantially reduce cataplexy with relatively few side effects.

**Approach to Sleep Disorders in Children**

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Identification of sleep problems in children is important because there is very strong evidence from the literature to suggest a link between sleep disorders and physical, cognitive, emotional, and social development. Children with neurodevelopmental problems, learning differences, or behaviour problems may be at heightened risk for sleep problems compared with the general paediatric population. Paediatricians, paediatric subspecialists, and other health care practitioners are in an ideal position to identify sleep problems and disorders in children. Parents may not volunteer information about their child’s sleep, or they may not appreciate the potential relationship between sleep problems and daytime behaviour. For these reasons, clinicians should incorporate questions about sleep into routine health assessment for children of all ages. Sleep problems present most commonly in the outpatient setting, but the hospitalised child may develop sleep problems during an acute illness, or chronic sleep disorders may come to medical attention during hospitalisation. This presentation will discuss the approach to taking a structured sleep history, describe specific sleep problems that may present during childhood, and explain indications for further diagnostic testing. This will enable the participants to understand the basic parameters, epidemiology and classification of sleep disorders in children, know how to take a structured sleep history and explain indications for further diagnostic testing.

**Sleep-Disordered Breathing in Children**

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Children of all ages can have a sleep-disordered breathing (SDB), just like adults; however, there are some differences in the pattern of causes and symptoms. Sleep in children with sleep-disordered breathing is very different from sleep in normal children. The increase in upper airway resistance during sleep can be extreme, and can lead to a markedly increased work of breathing associated with snoring, obstructive sleep apnoea and/or obstructive hypoventilation resulting in sleep disruption, hypoxia, and hypercarbia. The definition of SDB in children and the range of manifestations including the most common cause adenotonsillar hypertrophy will be discussed in detail. Other causes such as generalised hypotonia, as in patients with Prader-Willi syndrome, congenital central hypoventilation syndrome, and finally the treatment of SDB in children including surgery and CPAP will also be discussed.

**Parasomnias: Common sleep disorders in children**

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Parasomnia is a common sleep problem in children. Parasomnia can be sub-classified into disorders of arousal from non-rapid eye movement (NREM) sleep and parasomnias associated with rapid eye movement (REM) sleep. Arousal disorders from NREM sleep consist of several common disorders in children such as confusional arousals, sleep terror and sleep walking. Parasomnias associated with REM sleep include a common disorder like nightmares and a rare condition in children such as REM sleep behaviour. These episodes can be precipitated by stress, sleep deprivation, anxiety and environmental noises. Diagnosis of parasomnia is done by obtaining a standard clinical history with emphasis on detailed description, timing, and response to intervention. There is no need for a sleep study in children with simple parasomnias. A referral to a sleep centre is indicated in children with unusual presentations, persistent parasomnia, violent behaviours or symptoms of other sleep disorders. Polysomnography may demonstrate precipitous arousals from slow-wave sleep. In addition, a sleep study can help to identify co-existing sleep disorders which could potentially precipitate arousals, e.g., obstructive sleep apnoea. Treatment is reassurance and good sleep hygiene in mild cases. This presentation will enable participants to define and classify parasomnias as well as to differentiate between parasomnias and seizure/epilepsy in children.
Acute Ventilatory Failure Complicating Obesity Hypoventilation: Update on a “Critical Care Syndrome”
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Obesity can result in serious complications, including obesity hypoventilation syndrome (OHS). OHS patients may present with acute-on-chronic ventilatory failure, necessitating acute care management. This presentation will discuss the recent literature on acute ventilatory failure in OHS patients. Obese subjects can develop acute hypercapnic respiratory failure (AHRF) and sleep hypoventilation due to disorders in lung mechanics, ventilatory drive, and neuro-hormonal and neuro-modulators of breathing. Although there are no clearly defined predictors for OHS patients who are likely to develop AHRF, most such patients are middle-aged (mid-50s), morbidly obese, and have daytime hypercapnia, hypoxaemia, and low serum pH values. Immediate ventilatory support, without sleep study confirmation, is necessary in most such patients. Patients with respiratory acidaemia (pH < 7.30) or altered mental status may require intensive care unit monitoring. Non-invasive positive pressure ventilation (NIPPV) is the recommended initial ventilatory support which must be closely monitored. Prompt initiation of NIPPV reduces the need for invasive mechanical ventilation and rapidly improves the levels of blood gases. Obese patients with sleep hypoventilation have an increased risk of AHRF. Early diagnosis and implementation of NIPPV is recommended for these patients.

Central Sleep Apnoea
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Central sleep apnoea (CSA) occurs when both airflow and respiratory effort are absent. Recurrent central apnoeas are the main finding in central sleep apnoea syndrome (CSAS). These occur when the inhibitory input to the respiratory centre exceeds the excitatory input. CSAS is uncommon, occurring in approximately 4% of the population. The mechanism causing CSA is primarily related to removal of the wakefulness drive to breathe as well as unmasking of a Pco2 sensitive apnoeic threshold. In normal sleep, the ventilation decrease and hence Pco2 level slightly rise. The main control of ventilation during sleep is through the Pco2 level. In patients with CSA, Pco2 levels decrease to below the apnoeic threshold leading to temporary cessation of breathing which in turn raises the Pco2 to the normal level when the ventilation starts again. CSA could occur physiologically at sleep onset, but most often is a pathological process. Causes include heart failure, stroke, brain stem disorders, congenital alveolar hypoventilation syndrome and muscle disorders. Clinically, patients present with features similar to obstructive sleep apnoea with poor sleep, morning headache, daytime somnolence and nocturnal shortness of breath. In sleep study, CSA is diagnosed when more than 50% of the apnoeic events are central. Management of CSA includes finding the underlying cause like heart failure, hypothyroidism, brain stem lesions or muscle disease and managing it. CPAP therapy is used if CSA is associated with a significant amount of obstructive apnoea. Patients with hypercapnic CSA will benefit from bi-level ventilation. Optimising the treatment of heart failure in patients with CSA will improve the associated sleep disordered breathing. The role of oxygen and respiratory stimulants is less clear.

Polysomnography
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Polysomnography (PSG) is an excellent tool for evaluating sleep and sleep related disorders which utilises multiple physiological measures. These include brain waves (EEG), ocular movements (EOG), skeletal muscle activities (EMG), respiratory monitoring (airflow, effort, snoring), cardiac activity (ECG) and pulse oximetry (SaO2). In addition, audio and video recordings are made during the test. PSG gives an opportunity to correlate a variety of events occurring in separate physiological systems during different sleep stages and wakefulness. Scoring of sleep stages (NREM – N1, N2, N3 and REM) and wakefulness can be performed with the help of EEG, EOG and Chin-EMG activities which can be recorded by means of small surface electrodes through a conductive medium (gel). Appropriate sensors are used to monitor respiration. This includes thermal sensors for oro-nasal airflow, strain gages for respiratory effort (chest/abdomen movements) and dynamic snore microphones for snoring signals. Alternatively, a nasal pressure transducer can be used to register nasal airflow and snoring. Leg movements can be monitored by recording tibialis anterior muscle activity (EMG). ECG monitoring is essential to detect abnormal arrhythmias and cardiac activity. Sleep disordered breathing (SDB) such as apnoeas and hypopnoeas can be detected by a series of abnormally diminished airflow or cessation of airflow for a minimum duration of 10 seconds. These need to be correlated with other physiologic variations (to fulfill the criteria) such as drop in SaO2, arousal in EEG and other skeletal muscle movements along with abnormally heavy snoring. Audio/video recording is always advised for a better understanding of different types of parasomnias and nocturnal seizures.
Forthcoming Medical Conferences, Courses and Workshops


28–29 November 2011: The First International Nursing Conference: Innovations in Nursing Education & Practice Leading to Quality of Care. Sultan Qaboos University, Muscat, Oman
Website: web.squ.edu.om/nursing/

4–5 December 2011: Pre-Congress Workshop on Infection Control. Ministry of Health & Sultan Qaboos University, Muscat, Oman.
Website: www.moh.gov.om/ICITD2011

4–8 December 2011: 3rd International Congress on Infectious & Tropical Diseases and 6th GCC Conference on Infection Control. Ministry of Health & Sultan Qaboos University, Muscat, Oman.
Website: www.moh.gov.om/ICITD2011

4–8 December 2011: Diabetes Medical Congress. Dubai, United Arab Emirates.
Website: http://www.worlddiabetescongress.org/

8–11 December 2011: 15th World Congress on Controversies in Obstetrics, Gynecology & Infertility (COGI). Sanya, China.

Website: http://www.nephrology.emanuae.com

Website: http://www.wonca-dubai2011.com

11–14 January 2012: 2nd Pan Arab Endodontic Conference. Dubai, United Arab Emirates.
Website: http://paec2012.com/index.html


Website: http://www.woc2012.org/index.html

18–20 January 2012: International Congress on Malaria Elimination (ICME). Kish, Hormozgan, Iran.
Website: http://www.icme2012.ir/en

Website: http://www.continuingeducation.net/coursedetails.php?program_number=1023

Website: http://www.arabhealthonline.com/home/

Website: http://www.ssha-conferences.com/

28 January–1 February 2012: 8th International Scientific Conference for Medical Students in GCC Countries. Sultan Qaboos University, Muscat, Oman.
Email: rpe@gcc8medconf.com or rpe.oman@gmail.com

Website: http://www.apchf2012.com

6–8 February 2012: 3rd International Conference of Quality Management in Healthcare. Sultan Qaboos University, Muscat, Oman.
20–23 February 2012: Healthcare India. New Delhi, India.
Website: http://www.healthcareindia2012.org

Website: http://www.sith.itb.ac.id/en/

22–23 February 2012: Advanced General Medicine Conference: Pulmonology, Oncology, Haematology, Critical Care, Dermatology, Nuclear Medicine, Metabolic Diseases. Sultan Qaboos University, Muscat, Oman
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Thanks to Reviewers

2010–2011

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سنجيت نارانج

جهاز لرؤية المنزلق لقياس سلامة الفص الحنجرى الرأيع بعد جراحة الغدة الدرقية

مؤيد احمد

بتغطية التطعيم ضد التهاب الكبد الفيروسي البائي والاستجابة المناعية له عند الأطفال سن

سيد مؤيد الافيان

رد على: البطن الحادة كعرض لحمى الدنك النزفية

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- السياط الطبية الخفيف - مراجعة جديد نظام الصحية في عمان: تجربة المنطقة الداخلية
-nodified تأثير واسع النطاق على الطيات العاطفية في المدارس الأشياء
- السياط على المعلومات، الرعاية الصحية العامة، الممارسات المبتكرة على الدبابات وجرح الأذن والأذن والجدر
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- الوصف البيولوجي، الوصف الأول، في منطقة عمان
- حالة كاذبة في الحال
- هامات طفيلة مرضية مرضية
- موقع النقطة المحيطة بالがありました شديد
- العلاقة بين حالة مرضية ورضية
- معايير المثلية القرنية - كم سالك كجم
- ووجهة نظر
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