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The peer-review process for journals in the biomedical sciences; love it or loathe it, it won't go away!

Brian L Furman

All of us who work as scientists have experienced the joys, as well as the trials and tribulations of the peer review process. I would be surprised if there are any among the readership of this editorial who have not received a letter or e-mail from an editor informing them that their paper has not been considered suitable for publication – I certainly have! Such letters evoke the natural response of disappointment, which may turn to rage on subsequent reading of the reviewers' reports. This may be followed by incredulity at the sheer stupidity of the reviewers in their incapacity to understand the manuscript and its importance! While such incompetence on the part of the reviewers is possible, it is relatively unlikely and this editorial attempts to provide a critical appraisal of the process whereby these decisions are taken. The peer review process has been hotly debated, including the 2006 online debate in Nature, to which I shall make several references. While trying to be impartial, I must declare that I am part of the process, having been an author since publication of my first paper in 1969, a regular reviewer since around 1975 and a member of several editorial boards. I shall briefly describe the process, then discuss its pitfalls and finally try to suggest how it may be improved.

The process

Following submission of the paper, an editor will be assigned. Depending on the journal, the editor may form an opinion on the suitability of the manuscript for the particular journal but will usually identify and invite a number of suitable reviewers who have the relevant expertise. The number of reviewers will vary depending on the journal but will be at least two, commonly three and sometimes up to five. At the point of invitation, reviewers will receive the title and the abstract of the paper, in order to inform their decision as to whether they wish to undertake the review. After accepting the invitation, reviewers are given a date by which their reviews should be submitted; again this varies among journals but is usually 2 – 4 weeks from the date of accepting the invitation. Reminders are usually issued a short time before the due date. Once all the reviews have been submitted, the editor will make a decision (acceptance, minor revision, major revision, rejection) based on these reports. Where there is dissent among the reviewers, the editor will sometimes invite additional reviewer. In my experience, such dissent is infrequent and there is usually sufficient agreement with sufficient detail in the comments to inform the editor's decision.

What are reviewers asked to do?

Reviewers are expected to judge the manuscript on the basis of novelty and scientific quality. Commonly, they are asked if the topic is worthy of investigation and asked either to provide an overall score or to suggest if the manuscript quality falls within the top 10%, 20% etc. They are then expected to provide detailed comments covering the methods, experimental design, results and discussion; they are also expected to comment on any ethical issues relating to the use of animals of human subjects. The comments are intended to be constructive, so that manuscripts can be improved through, for example, reinterpretation, additional experiments or rewriting. Reviewers are also invited to make confidential comments to the editor; my view is that this should be used very sparingly and only when the reviewers have concerns relating to plagiarism or other ethical issues. Reviews are independent so that reviewers only see others' comments/recommendations once the editor has made a final decision on the fate of the manuscript.

Is the process necessary?

Following the 2006 Nature debate on the peer review process and an article by Smith (2006), one might form the view that because of its flaws, including reviewer bias and lack of transparency, as well as the lack of evidence that it results in the publication of better quality manuscripts, the process should be abandoned and that journals should simply publish all articles received; the scientific community would then judge their quality. Arguments could be developed to support this view;

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for example, it would allow unhindered repetition of experiments so that observations could be tested more rigorously. It would also allow the publication of negative findings which are just as important as positive results but against which the present process is bias. My own view is that removal of the review process would clutter an already crowded literature with poor quality papers that busy scientists would need to read to gain a balanced view of the literature; improvements to encourage publication of negative results and corroboration of reported observations could be accommodated within the present process by modifying journal policies. Experienced reviewers will have seen the huge number of flawed papers that have been rejected for very good reasons. My experience is that the peer review process eliminates the poorest papers and frequently results in enhancement of those that are eventually published. However, I readily accept that the peer review process does not guarantee the value, validity or importance of a manuscript; these aspects may take many years to emerge.

Pitfalls in the process

Demands on reviewers

When done properly, reviewing a manuscript is a hugely time-consuming activity, requiring detailed reading of the article, including careful scrutiny of the 'materials and methods' section, to ensure that these are appropriate and valid. When looking at the results the reviewer should determine if statements in the text are supported by the data presented in the figures and tables and will consider if these data are of adequate quality and quantity to support/refute the hypothesis being tested. The 'discussion' will then be examined to determine if the results have been interpreted correctly and if additional experiments are essential. I know of no evidence that the time required for a comprehensive review has ever been quantified; I normally allocate half to two working days, depending on the complexity of the manuscript and how close it is to my specific expertise. Wager *et al.*, (2002) suggested allocating two to five hours, with eight to twelve hours for a first time review but acknowledged that a review may take up to 48 hours. Reviewers are mostly very busy, even those of us who are retired (!) and some may read the paper rather superficially resulting in an inadequate judgement. Variability in review quality was highlighted by a former editor of the BMJ (Smith, 2006).

Reviewer bias

While the authors will not know the identity of the reviewers, the names, laboratories and countries of origin of the authors are clearly stated at the top of the manuscript. This may lead to a prejudiced report on the paper; this prejudice may be either favourable or unfavourable in deciding the manuscript's fate. At one extreme, the reviewer may decide that the paper emanates from a good laboratory with a well-known senior author and may thus be favourably disposed towards the paper before reading one word. At the other extreme, the paper may have come from an unknown laboratory in a developing country. Sometimes, although the paper may have originated in an established laboratory with a well-known senior author, the reviewer may have adverse view of the work of that particular individual. The anonymity of reviewers is sometimes taken as a right to make comments that would not be made if the reviewers' identities were known.

How might the process be improved?

Blinding of reviewers to the authors

There is no evidence that this improves the quality of the reviews; this may emanate from the difficulty in fully hiding authors' identities.

Open review

There are strong advocates of open peer review, with some journals (the BMJ and the numerous BMC medical journals) operating an entirely transparent peer-review and publication process, whereby authors

and reviewers know each other's names and addresses; moreover, BMC medical journals publish the reviewers' reports. The esteemed journal Nature, which rejects 93% of the papers it receives, undertook an experiment whereby in parallel with the standard review process, it displayed submitted papers, if the authors agreed, on an open server and invited public comment, including encouraging relevant scientists to participate (Greaves *et al.*, 2006). No huge enthusiasm for this particular 'open peer review' process emerged from the study and there did not appear to be any evidence that the process offered advantages over the standard system in terms of the quality of the comments posted. However, this was just one experiment that a) was based on an atypical journal and b) involved no papers in the areas of biochemistry, chemical biology, chemistry, genetics/genomics, medical research, or microbiology, The Nature debate on peer review highlighted other forms of open peer review (Koonin *et al.*, 2006; Koop and Pöschl, 2006; Sandewall, 2006). Perhaps some version of these processes may become increasingly accepted by the biomedical scientific community. However, while there is no scientific evidence to support the validity of the traditional process, one may equally argue that replacing it by another system should be supported by evidence that it would produce a better outcome.

Rewarding reviewers

Some journals offer financial rewards to reviewers, while others offer a period of access to the journal or to databases such as Scopus. My own view is that as a scientist, one has a responsibility to undertake peer review and that financial and other incentives are unnecessary. Reviewing also offers one opportunity for continuing professional development; indeed, some journals offer formal CME points for good reviews.

Training of reviewers

Learning to review papers should be part of one's training as a scientist. This arises from journal club meetings of research groups, from writing papers and from the feedback one receives from reviewers after submitting a manuscript for publication.

Conclusion

Although far from perfect, peer-review remains an essential part of the scientific publication process. Nevertheless, the scientific community should retain an open mind about how the process could be improved but should seek evidence on the value of any improvements, while acknowledging that we also need evidence for the effectiveness of the current process.

Keywords: peer review; Nature debate; reviewer bias; open review; improvements to peer review process; training of reviewers; blinding of reviewers

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Comprehensive review of mnemonic devices and their applications: State of the art

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Abstract: Mnemonic devices can be defined as learning strategies which can often enhance the learning process and later the recall of information. On the other hand, mnemonic systems are special techniques or strategies consciously used to improve memory, they help employ information already stored in long-term memory in order to make memorisation an easier task. There is no doubt that mnemonic techniques are one of the most important methods and methodologies used in education. However, nowadays these methods seem to be unremembered and seldom used by teachers or students. There is a deficit in the actual reviews on this subject. In this article we review mnemonic methods from the point of view of teaching and learning science subjects. This article is the first work in literature that refers to and emphasises various and complex aspects of mnemonic devices applications in didactic practice like science learning and teaching, helping students with disabilities and behaviour problems and second language acquisition.

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Keywords: Mnemonic devices, methods, students with disabilities, behaviour problems, second language

Introduction

The word "*mnemonics*" is derived from the μνημονικός (mnēmonikos), meaning "*of memory*", or "*relating to memory*" and is connected with Mnemosyne – the Greek titan, goddess of memory that represented memory ("*remembrance*") in Greek mythology.[1]

The idea of mnemonics is application in developing better ways to take in (encode) information, so that it is much easier to remember (retrieve)[2] it. Therefore, mnemonic devices can be defined as systematic procedures for intensification of memory. Hence, mnemonic devices ought to be understood as learning strategies which can often enhance the learning and later the recall of information.[3] The main idea in mnemonic strategies is to find a connection between a new piece of information and the one that students have already locked in long-term memory. If the connection the students make is strong enough, the memory will last for a very long time, because of the fact that the mnemonic strategy carefully links it to things that are very familiar according to these procedures and they can be powerfully effective.[2] What is more, further mnemonic devices can be incorporated for the things that require recall. These strategies are also a useful way of improving memory in students who exhibit difficulty with remembering things. Although the mnemonic devices are not an educational panacea, they can play an important part in improving memory for learning or teaching processes.

There are various types of mnemonic methods described, yet a suitable classification and nomenclature system of those methods are lacking. Because of this problem it is very important to note the basic distinction between mnemonics that primarily involve organising operations and those that primarily involve encoding operations. An organising operation is one that associates or relates in memory units of information that at first appear unrelated.[3] Furthermore, an encoding operation transforms a unit of information into some other form that can be fit into some organisational scheme. Mnemonic devices have been differently classified by different authors, e.g. Thompson in 1987[4] arranges mnemonic strategies into five classes: linguistics, spatial, visual, physical response and verbal methods. On the other hand, Oxford in 1990[5] identifies four major strategies: namely, creating mental linkage, applying images and sounds, reviewing well, and employing action. In turn, Baddeley in 1999[6] described that mnemonic devices can be classified into visual imagery strategies and verbal strategies.

Methods

The primary aim of this article was to review the articles related to mnemonic devices and its applications in learning and teaching of science subjects, teaching of students with disabilities and behaviour problems, and in second language acquisition.

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The classification method used in this study was the method adopted by Bellezza in 1981[3] (Fig. 1), which seems to be more comprehensive in our opinion.

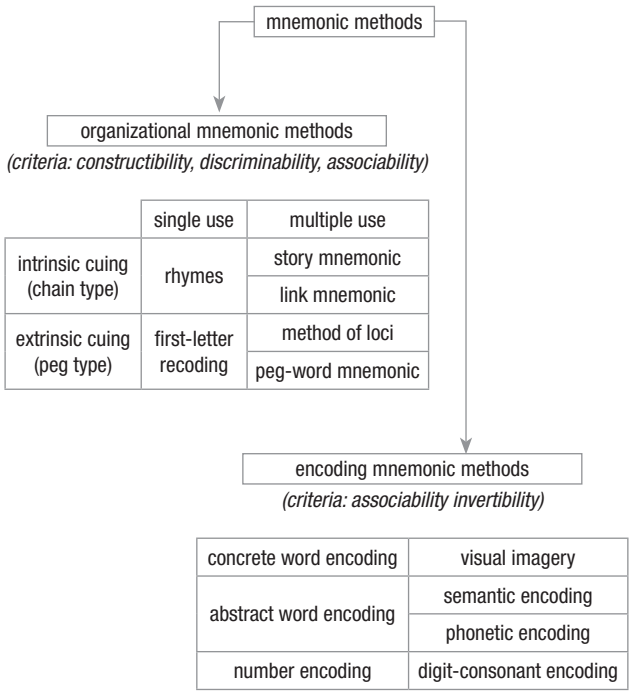

Fig. 1: Classification of mnemonic methods – based on.[3, 7]

We reviewed the theoretical and empirical literature on mnemonics as memorised tools, published over the past half century, primarily focusing on research in pedagogical and educational journals. We examined articles related to the mnemonic methods and methodologies according to: 1) Mnemonic methods as didactic tools (9 articles); 2) Application of mnemonic devices in learning and teaching of science subjects (30 articles); 3) Application of mnemonic methods in teaching students with disabilities and behaviour problems (9 articles); 4) Application of mnemonics devices in second language acquisition (7 articles). For our studies we applied Google Scholar due to the fact that it has been well received among the research community. Moreover, Google Scholar offers free, universal, and easy access to scientific literature coupled with the perception that it covers the social sciences and the humanities better than other traditional multidisciplinary databases.[8]

Results and Discussion

Mnemonic methods as didactic tools

It must be emphasised that the mnemonic methods are not a general teaching method or a curricular approach.[2] The idea of mnemonic strategies is so specific that they are intended to be used to enhance the recall of the components of any lesson for which memory is needed. From the didactic point of view, mnemonic strategies are memory strategies and not comprehension strategies.[2] As was mentioned earlier, many articles provide evidence that the application of a mnemonic method by students or pupils increases their results in comprehension tests.[9,10] This situation occurs because they are able to remember more and it can be applied in comprehension tests. For example, Chase and Ericsson in 1981 and 1982 described that regular college students can attain world-class memory performance after extensive practice and proposed skilled-memory theory as an account for how ordinary people can acquire exceptional memory.[11,12] On the other hand, due to the exceptional memory performance, Wilding and Valentine (1997) reported that the skilled-memory theory did indeed account for truly exceptional memory performance involving specific types of materials, such as digits.[13] Moreover, these authors also proposed evidence for the existence of naturally superior memory, whereby some people's memory for specific materials had never been truly exceptional, but consistently well above average for several different materials tested. Besides, these subjects reported that they did not use mnemonic encoding strategies.[13] Based on this observation, it can be ascertained that mnemonic strategies are not comprehension strategies, but only memory strategies/methods.[14]

Application of mnemonic devices in learning and teaching of science subjects

Approaches to the science of learning are very different. Mnemonic strategies can be incorporated into the elements that require recall.[15] Educationally, mnemonic methods can have a significant impact on studying or teaching important information, and can improve recall and boost the student's self-confidence which in the scientific field is important because of the fact that the ability of recalling new pieces of information is often more difficult due to the unfamiliarity with the content.[16] Mnemonic procedures and materials are valuable in classroom teaching, but the question is how effective self-initiated mnemonic strategies can be for all learners.[17]

Mastropieri and Scruggs in 1998[2] have found that mnemonic strategies can be used to enhance science learning when the curriculum involves a handbook / lecture format or when the curriculum involves a hands-on, inquiry learning format. Even though these approaches to science learning are very different from each other, mnemonic strategies can still be incorporated for the elements that require recall.

In science courses (Chemistry, Biology, Physics and also Mathematics) there are many examples of mnemonic devices, but describing these examples is beyond the scope of this review. A list of selected popular examples of mnemonic devices in science courses is presented in Table I.

Table I: Examples of mnemonic devices applications in teaching and learning science.

Science Subject	Example	Source(s)
Chemistry	Monosacharides	18, 19, 20
	Thermodynamic functions	21, 22, 23
	Gas laws	24, 25
	Indicator Colours	26, 27
	Mole and Molarity	28
	Electronic configurations of atoms	29, 30, 31
Biology	Vertebrates: Fish, Amphibians, Reptiles, Mammals, And Birds	2, 32
	The Krebs cycle	33, 34, 35
	The Calvin Cycle	36
	The order of taxa in biology	37, 38
Physics	Colour coding on electronic resistors	39, 40
	The colors of visible light (colours of the rainbow)	41, 42
	Speed of light in metres per second	43
	Maxwell relations in thermodynamics	44
	Metric prefixes	45
Mathematics	Pi number	3, 46
	Correct order of operations of an algebra	47
	Number for sequences	48
	Trigonometry	49, 50

Application of mnemonic methods in teaching students with disabilities and behaviour problems

There is no doubt that mnemonic strategies organise and integrate the transformation of information which is difficult to remember into something that is more meaningful for individuals to recall at a later date by using associations between the new item of information and the one previously learned in long term memory.[16,51,52,53] Mnemonic strategy instructions for students with learning disabilities and other mild disabilities have been studied experimentally for almost 20 years.[54] Students with learning disabilities and other special needs may be at particular risk of failing at school. As was described by Mastropieri *et. al.* in 1998[2] teachers should teach students how to remember as well as what to remember. This can be done by a variety of strategies, but most useful ones were: the keyword method, the pegword method, and letter strategies. Systematic instruction makes use of mnemonic methods not only for remembering important information, but also for systematic instruction in the independent use of mnemonic strategies. They can be important factors in determining school success for students with learning and memory problems.

What is more, students with learning disabilities have been taught to successfully generate mnemonic strategies independently. Research findings indicate that they learn more content in shorter instructional time periods when mnemonic strategies are developed and presented by teachers.[55] This does not indicate that teachers should not encourage students to develop strategies independently, however, it does imply that teachers should think carefully about the allocated time for specified subject areas and content to be covered. Hence, if there is sufficient time for students to learn to develop and generate their own strategies, teachers should encourage them to do so[56]. This clearly shows that once mnemonic materials have been developed they can be used time and again.[28]

Application of mnemonic devices in second language learning

Interestingly enough, the effective use of encoding technique, which relies on phonetic encoding, can be frequently found in teaching foreign language vocabulary.[57,58,59] This example of use despite appearing to be strange and difficult at first sight, is indeed very easy. In this approach a foreign word is presented and its English translation must be remembered. The English word, the "keyword," that sounds like some part of the foreign word to be learned is found. This is possible, when the phonetic encoding of the stimulus unit occurs. The next step is forming the mental image of the keyword interacting with the English translation of the foreign word. Hence, the correlation between the foreign word and its English equivalent can be based on two associations: 1) phonetic (acoustic) and 2) visual imagery.[3]

The application of mnemonic studies in second language learning by the means of phonetic (acoustic) association was first described by Atkinson in 1975.[59] He proposed linking acoustic mnemonic to imagery mnemonic in order to help students to learn Russian. The students were given an English word that had a similar pronunciation to the Russian word. Then, students were told to imagine that word interacting with the true definition of the word. Not only did this spark interest in mnemonics as an aid to teaching language, due to his successful results, but also his final remarks in the paper, where he stated that this technique might be very useful for these students who find language learning especially challenging, led to a whole new application of mnemonics.[60, 61]

While mnemonic devices are characterised by numerous advantages, there are some disadvantages. The advantages and disadvantages of mnemonic methods are presented in Table II.

Table II: Advantages and disadvantages of mnemonic strategies.

Advantages	Disadvantages
• Procedures for intensification of memory; • Extremely effective in helping people to remember things; • Own prepared mnemonics by students outperform the results in comparison to students in free-study conditions; • Often enables information to be better retained in memory; • Memory strategies; • Is not as dependent as a memory schema	• Are not comprehension strategies; • Low or lack connection between the conceptual content and the material being learned; • Students' performances may be lower than when teachers supply the strategies; • Are focussed only on certain aspects of their operation; • Are not teaching and learning methods

Conclusion

This review has looked at various perspectives of the value of mnemonic devices. From a cognitive perspective, mnemonic strategies are effective because they form an effective acoustic-imaginal link between the stimulus and response.

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E-cigarettes: Facts and legal status

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Abstract: The sale of tobacco-based cigarettes has declined in western countries, and 'Big Tobacco' is trying to make up the deficit in profits from the developing world. The recent introduction of e-cigarette, in which they have invested both their hopes and their finances, has been a boon to them as it serves to confuse smokers and non-smokers about the real issues relating to the toxicity, dangers, and the promotion of nicotine addiction especially among youths who have not previously smoked cigarettes. E-cigarettes cause inflammation and damage to epithelial cells in human airways and increased risk of infection. E-cigarette vapour contains more carcinogens like formaldehyde and acetaldehyde compared to a regular cigarette. Long-term vaping is associated with an incremental lifetime cancer risk. E-cigarettes are neither safe nor effective in helping smokers quit; there is enough evidence to caution children, adolescents, pregnant women, and women of reproductive age about e-cigarette's potential for long term consequences to foetal and adolescent brain development that sub-serve emotional and cognitive functions. The nicotine effects that cause modification of late CNS development constitute a hazard of adolescent nicotine use. The American Heart Association (AHA), Food and Drug Administration (FDA), World Health Organisation (WHO) and two-thirds of the major nations in the world discourage the promotion of e-cigarettes as an alternative to proven nicotine-addiction treatments. Doctors, health care workers, and medical students should be armed with the facts about e-cigarettes, its dangers, and the legal status concerning its use, in order to be able to offer proper counselling to patients and adolescents, in particular, with special reference to the Malaysian context.

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Introduction

Electronic cigarettes (e-cigarettes) or electronic nicotine delivery systems, have gained popularity among smokers, especially the youth, world-wide. Despite the current legal barriers, the use of e-cigarettes has increased world-wide and among Australian smokers.[1] In the US, e-cigarettes have surpassed snus in adoption rate, even before launching of promotion campaigns by major tobacco companies, suggesting that these companies have tapped into smokers' intuitive preference for potentially harm-reducing products, probably due to the product design. They anticipate that e-cigarette use is likely to increase further in the next few years.[2] Giant tobacco companies are buying up e-cigarettes producers, in order to have their piece of the pie of a global market estimated at USD 3 billion.

Most smokers believe e-cigarettes are safer than regular cigarettes; many use it hoping that it would help them quit smoking.[3] Cheapness of e-cigarettes compared to regular cigarettes also contributes to its popularity. Available data suggest that smokers in the United States of America (USA) are not waiting for a consensus view from health authorities to decide if they should switch to e-cigarettes. E-cigarettes are likely to gain users in the next few years regardless of the opinions of the scientific community.[2] Kanda *et. al.* conducted an e-mail survey of North Carolina physicians and found that two thirds (67%) of the surveyed physicians considered e-cigarettes a helpful aid for smoking, and 35% recommended them to their patients. Physicians were more likely to recommend e-cigarettes when patients asked about them or when the physician believed e-cigarettes were safer than smoking standard cigarettes.[4]

It is apparent that medical students and physicians need evidence-based guidance on e-cigarettes that will help ensure their smoker patients receive evidence-based recommendations about the safety and efficacy of e-cigarettes. They would also need to counsel non-smokers and especially the youths contemplating using e-cigarettes about their potential danger to health, and educate them about the legal status of e-cigarettes in Malaysia and the rest of the world.

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Facts about e-cigarettes

History

A Beijing Chinese pharmacist, Hon Lik first developed e-cigarettes in 2003 as a smoking alternative for traditional tobacco smokers.[5] Following its introduction in 2007, the e-cigarette has become a commercial success in the USA. Big tobacco companies – Lorillard, Atria and Japan Tobacco have moved into the e-cigarette market in UK, US and Japan. With money and political clout, 'Big Tobacco', has become a major player for e-cigarettes in the global market, and is viewed by them as a solid hedge against a half-century decline in adult smoking rates. They actively promote the idea that the benefits of e-cigarettes outweigh their risks.

What are e-cigarettes?

E-cigarette is an electronic re-chargeable battery-powered nicotine delivery system that simulates tobacco smoking. It appears like a cigarette, has a mouthpiece, a heating element, a disposable or refillable cartridge, and an atomiser that produces an aerosol (vapour) instead of smoke which the user inhales. A LED light at the end of the device glows when the smoker inhales to simulate real smoking. There are disposable and reusable versions. E-liquids comprise a mixture of propylene glycol, glycerol, nicotine, and flavourings. Various E-liquids are available with or without nicotine, propylene glycol, and flavours like tobacco, mint and fruit. Experienced smokers can achieve nicotine blood levels similar to tobacco smoking.[7]

Impact of e-cigarettes on health

E-cigarettes are being promoted as an aid to quitting cigarette smoking, and a safer long-term alternative to tobacco cigarette smoking, but the question is whether e-cigarettes promote addiction?

E-cigarette as an aid to quitting cigarette smoking

There is very limited data on whether e-cigarettes help individuals quit cigarette smoking. A prospective proof-of-concept study by Polosa *et. al.* showed that the use of e-cigarette substantially decreased cigarette consumption without causing significant side-effects in smokers not intending to quit.[8] Adkison *et. al.* found e-cigarettes, with or without nicotine, were modestly effective at helping smokers quit, with achievement of similar rates of abstinence as with nicotine patches. Uncertainty exists about the place of e-cigarettes in tobacco control and their overall benefits and harms at both individual and population levels.[9] Addiction Magazine 7 has reported that among smokers who have attempted to stop smoking without professional support, those who used e-cigarettes were more likely to report continued abstinence than those who either used a licensed nicotine replacement therapy product that they had bought over-the-counter, or those who did not use any aid to help quit smoking.[10]

A study on the use of e-cigarettes among state tobacco quit line callers found that nearly one-third of respondents reported ever using or trying e-cigarettes. Of those who had tried e-cigarettes, over six in ten (61.7%) reported using them for less than one month. Reasons for using e-cigarettes included help with quitting tobacco smoking (51.3%) or using it to replace other tobacco products (15.2%). E-cigarette users (both those who had used e-cigarettes for more than one month and less than one month) were significantly less likely to quit tobacco smoking seven months after calling a state quit line compared with participants who had never tried e-cigarettes (30-day point prevalence rates: 16.6% and 21.7% vs. 31.3%, $p<.001$).[11] A prospective 6-month pilot study on the effect of e-cigarette on smoking reduction and cessation showed a substantial decrease in smoking and cessation without causing significant side effects in smokers not intending to quit. However, large and carefully conducted RCTs will be required before a definite answer about the efficacy and safety of these devices can be formulated.[13]

Is e-cigarette a safer long-term alternative to tobacco cigarette smoking?

Researchers at the National Jewish Health in Denver have provided strong evidence that the liquid used in e-cigarettes, whether it contains nicotine or not, has negative effects on the airways and on the lungs. Its vapour can damage human airway epithelial cells and increase the risk of infection. The researchers noted a significant increase in the level of IL-6 protein from the cells, which indicates an immune response to the e-cigarette exposure. The epithelial cells were damaged after only a few minutes of exposure and the immune response lasted up to 48 hours. These cells responded quickly to the presence of e-cigarette liquid or vapours by producing IL-6 protein, which contributes to the lung inflammation and injury.[14] This study confirms the real dangers of e-cigarettes and the need to prevent e-cigarettes falling into the hands of children and teenagers who falsely assume that they are safe.

Researchers commissioned by Japan's Ministry of Health have found carcinogens such as formaldehyde and acetaldehyde in the vapour produced by several types of e-cigarette liquid. These carcinogens were present at much higher levels than those found in the smoke from regular cigarettes. In one brand of e-cigarette, the level of carcinogens was 10 times more than the level contained in one regular cigarette; the amount of formaldehyde detected varied through the course of analysis. When the wire which vaporises the liquid gets overheated, higher amounts of those harmful substances were produced.[15]

Kosmider *et. al.* found that in many samples of the particulate matter of the aerosol of "vaped" e-cigarettes, more than 2% of the total solvent molecules had converted to formaldehyde-releasing agents that reached concentrations higher than those of nicotine.[16] This happens when propylene glycol and glycerol are heated in the presence of oxygen to temperatures reached by commercially available e-cigarettes operating at high voltage. How formaldehyde-releasing agents behave in the respiratory tract is unknown, but formaldehyde is a recognised International Agency for Research on Cancer group 1 carcinogen.[16]

In another study published in the New England Journal of Medicine, Jensen *et. al.*[17] observed that formaldehyde-containing hemiacetals, shown by others[18] to be entities that are detectable by means of nuclear magnetic resonance (NMR) spectroscopy, can be formed during the e-cigarette vaping process. Formaldehyde, a known degradation product of propylene glycol, reacts with propylene glycol and glycerol during vaporisation to produce hemiacetals molecules that are known formaldehyde-releasing agents and are used as industrial biocides.[19] Jensen *et. al.* found that long-term vaping is associated with an incremental lifetime cancer risk of 4.2×10^{-3}. This risk is 5 times as high compared with the risk associated with long-term standard smoking based on the calculation of Miyake and Shibamoto[20] or even 15 times as high based on the calculation of Counts *et. al.*[21] In addition, formaldehyde-releasing agents deposit more efficiently in the respiratory tract than gaseous formaldehyde, and thus carry a higher slope factor for cancer.

Some retailers have falsely claimed that e-cigarette is an effective nicotine replacement therapy and a smoking cessation aid endorsed by the World Health Organisation (WHO), but WHO's position is quite clear; it does not support e-cigarettes as a legitimate therapy to help smokers quit as there is a lack of conclusive scientific evidence to substantiate the efficacy, safety and quality of e-cigarettes. WHO calls on marketers of e-cigarettes to immediately stop their false and unproved claims about the safety of e-cigarettes, and encourages smokers to quit smoking using nicotine patches as an aid instead of e-cigarettes. In July 2014, WHO issued a comprehensive report on the harms of e-cigarettes and proposed options to regulate the import, sale and use of the products. This position is supported by the Singapore Ministry of Health.[22] E-cigarettes have also not been approved as a cessation aid by the Food and Drug Administration (FDA) that is responsible for assuring the safety, efficacy and security of drugs and medical devices in the United States. In January 2015, the California Department of Public Health (CDPH)

issued a Health Advisory warning to the public on the health risks posed by the marketing, sale and use of e-cigarettes, especially to children and young people.[23] Electronic cigarettes have so far not been proven to be either safe or effective in helping smokers quit. To date, there are no double-blind, placebo-controlled studies establishing the usefulness of e-cigarettes to help people quit smoking but there is enough evidence "to caution children, adolescents, pregnant women, and women of reproductive age" about e-cigarette use, as foetal and adolescent nicotine exposure has the potential to cause long-term consequences for brain development". WHO also advocates that e-cigarettes should be banned from indoor public spaces and has called on governments to ban the sale of e-cigarettes to minors, warning that they pose a "serious threat" to unborn babies and young people.[24]

Does e-cigarette promote nicotine addiction?

Animal studies

McDonald *et. al.* have reported that periadolescent nicotine administration to male Long-Evans hooded rats produces enduring changes in dendritic morphology of medium spiny neurons from nucleus accumbens. A subsequent behavioural experiment suggested that the observed anatomical changes are associated with enduring psychomotor differences. These findings indicate that periadolescent exposure to nicotine can result in long-lasting structural changes in the nucleus accumbens shell and are consistent with behavioural data suggesting that adolescent nicotine exposure may result in vulnerability to nicotine addiction in adulthood.[25] Bergstrom *et. al.* found that chronic nicotine exposure produces lateralised, age-dependent dendritic remodelling in the rodent basolateral amygdala,[26] that is generally thought to be involved in the acquisition and consolidation of emotional memory.[27] There is some evidence to suggest that prior nicotine produces lasting alterations of emotional memory that depend on BLA functioning, including auditory fear conditioning.[28] Persisting anxiety or stress as a consequence of smoking represents an important contributing factor to nicotine addiction.[29] Nicotine has been found to act as a typical drug of abuse in experimental animals and humans. It can function as an effective reinforcer of drug-seeking and drug-taking behaviour both in experimental animals and humans, under appropriate conditions. Interruption of chronic nicotine exposure produces withdrawal symptoms that may contribute to relapse.[30] In adolescent rats, nicotine-induced dendrite remodelling in the nucleus accumbens is rapid, persistent, and D1-dopamine receptor dependent.[31]

Slotkin *et. al.* found that nicotine administration in adolescent rats reprogrammes the subsequent response to nicotine treatment and withdrawal in adulthood. In males, prior exposure to nicotine in adolescence greatly augmented the increase in serotonin turnover evoked by nicotine given in adulthood, an interaction that was further exacerbated during withdrawal. The effect was sufficiently large to cause a significant depletion of serotonin stores, an effect that was not seen with nicotine given alone in either adolescence or adulthood. In females, adolescent nicotine exposure blunted or delayed the spike in serotonin turnover evoked by withdrawal from adult nicotine treatment, a totally different effect from the interaction seen in males. Combined with earlier work showing persistent dysregulation of serotonin receptor expression and receptor coupling, the results indicated that adolescent nicotine exposure reprogrammes future responses of 5HT systems to nicotine, changes that may contribute to life-long vulnerability to relapse and re-addiction.[32]

Adolescent nicotine induces persisting changes in the development of neural connectivity. Adolescent nicotine may induce a more addiction-prone phenotype, and the structures altered by nicotine also sub-serve some emotional and cognitive functions, which may also be altered. Dendritic elaboration and associated changes are mediated by activity-dependent synaptogenesis, acting in part through D1DR receptors, in a network activated by nicotine. The adolescent nicotine effects

suggest that modification of late CNS development constitutes a hazard of adolescent nicotine use.[33]

Studies in school children

Azzazola *et. al.*[34] studied tobacco use among middle and high schools in the United States from 2011-2014; they found tobacco use and addiction most often begin during adolescence and early adulthood. The Centre for Disease Control (CDC) in Atlanta and the FDA analysed data from the 2011-2014 National Youth Tobacco Surveys (NYTS) to determine the prevalence and trends of current (past 30-day) use of nine tobacco products (cigarettes, cigars, smokeless tobacco, e-cigarettes, hookahs, tobacco pipes, snus, dissolvable tobacco, and bidis) among U.S. middle (grades 6-8) and high school (grades 9-12) students. In 2014, e-cigarettes were the most commonly used tobacco products among middle (3.9%) and high (13.4%) school students. Between 2011 and 2014, statistically significant increases were observed among these students for current use of both e-cigarettes and hookahs ($p<0.05$), while decreases were observed for current use of more traditional products, such as cigarettes and cigars, resulting in no change in overall tobacco use. Consequently, 4.6 million middle and high school students continue to be exposed to harmful tobacco product constituents, including nicotine. Nicotine exposure during adolescence, a critical window for brain development, might have lasting adverse consequences for brain development, causes addiction, and might lead to sustained tobacco use. For this reason, comprehensive and sustained strategies are required to prevent and reduce the use of all tobacco products among youths in the United States.[34]

CDC has warned that e-cigarette use has more than doubled among U.S. middle and high school students from 2011-2012.[34] It considers this increased use by teens deeply troubling, as nicotine is highly addictive. Many teens who start with e-cigarettes, may be condemned to a struggle with a lifelong addiction to nicotine and conventional cigarettes.[35] Robert Preidt found that the number of young non-smokers who tried e-cigarettes had tripled in a span of 2 years.[36] The CDC report also found that non-smoking children who used e-cigarettes were nearly twice as likely to plan to start smoking tobacco cigarettes compared to those who never used e-cigarettes – about 44 percent versus 21.5 percent, respectively. CDC is concerned about nicotine use among the youth, regardless of whether it comes from conventional cigarettes, e-cigarettes or other tobacco products. Not only is nicotine highly addictive, it can harm adolescent brain development and cause lasting problems in thinking and memory.[36] Tobacco control efforts that have cut in half the youth smoking rate from 1997 to 2007, and have saved >8 million lives in the past 50 years, may be undermined by the pernicious introduction of e-cigarettes. The American Heart Association (AHA) has called for e-cigarettes to be subject to the same laws that apply to tobacco products, and for the U.S. government to ban the marketing and sale of e-cigarettes to young people.[37]

Tobacco advertisements increase teenagers' chances of smoking, and the greater the number of tobacco ad sources the more likely teens planned to start smoking. Celebrity endorsement of electronic cigarettes will have the same impact on today's youth that tobacco advertisements of the past, by Hollywood icons, had on today's adult smokers. Cigarette advertising encourages youth to smoke and should be banned. These findings highlight the need for the FDA to develop strong regulations regarding electronic cigarettes, as without these regulations, the use of e-cigarettes is bound to increase among teenagers, leading to a reversal of the success that has been achieved in tobacco control over the past years, especially among adolescents.[38]

E-cigarettes in Malaysia and its legal status in the region

Early this year, the Society for Research on Nicotine and Tobacco published the results of a household survey that revealed worrying data on e-cigarettes in Malaysia. Of the four lower and middle income countries surveyed, 21% of adult respondents in Malaysia compared to 10.9%

in Indonesia, 49% in Qatar, and 88.5% in Greece were aware or ever heard of e-cigarettes. The use of e-cigarette among those who were aware of e-cigarettes was 3.9% in Malaysia compared to 2.5% in Indonesia, 2.2% in Greece and 1.8% in Qatar respectively. The sample size and overall response rate for this Global Adult Tobacco Survey in each country was 8305 (Indonesia, 94.3%), 4250 (Malaysia, 85.3%), 8389 (Qatar, 98.5%), and 4357 (Greece, 69.6%) respectively.[39]

Another survey, the Malaysia Adult Smoker Survey (MASS), was conducted in June 2015 by Ipsos, a leading global polling company representing factasia.org[40] (an independent non-profit consumer orientated advocacy organisation representing the rights of adults in Asia who choose to enjoy smoking or other related forms of consumption of nicotine). This survey also showed distressing data; most Malaysian smokers (82 percent) considered e-cigarettes a "positive alternative" to regular cigarettes, and 75 percent of them stated they "would consider purchasing e-cigarettes from other channels or countries if the government were to restrict their availability in Malaysia. Currently, 26 percent of e-cigarette users obtain their e-cigarette products online where there are no recognised standards or quality regulations.

The latest reported number of e-cigarettes users in Malaysia is between 250,000 and 1 million; many vendors are thriving in this extremely profitable market by targeting the public with false advertisements that e-cigarette is a safer alternative to standard cigarette. Some medical doctors and administrators, ignorant of the true facts, appear to accept these false baseless claims made by e-cigarette manufacturers and retailers. Worried by the facts and figures on e-cigarettes, the Malaysian consumer associations are now demanding more effective regulations and enforcement.[41] It takes merely 0.15mg of nicotine to cause addiction, and there is a strong potential for e-cigarettes to cause nicotine addiction as the liquid nicotine concentrations stated in commercial products are often inconsistent with measured nicotine.[42]

Current regulations on e-cigarettes vary between countries, some have no regulations and others ban the devices totally.[43] It is estimated that in 2014, there were 466 brands of e-cigarettes and more than USD 3 billion were spent on it globally.[44] In 2015, around two thirds of major nations have regulated e-cigarettes in some way.[45] More than half of the world's population have access to it with its market increasing exponentially despite warnings by WHO.[46] Turkey was the first to ban e-cigarettes in 2008.[47] WHO reported a ban on e-cigarettes in 13 out of 59 countries that regulate them. A summary of the data collected by WHO from its survey is provided below[46]:

- Comprehensive advertising, promotion and sponsorship bans on e-cigarettes are in place in 39 countries (in which 31% of the world's population live)
- Use of e-cigarettes in enclosed public places is banned in 30 countries (35%);
- Premarket review is required by 19 countries (5%)
- Vendor licences are required by nine countries (4%)
- Policies on e-cigarettes sales to minors were confirmed by 29 countries (8%).

Many countries operate a two-tier system: nicotine and non-nicotine products i.e.:

- Hardware that does not contain nicotine is permitted;
- Refills without nicotine are permitted; and
- Refills with nicotine (or units sold pre-filled with a nicotine-containing refill) that require a medical license.

In May 2015, John Hopkin Bloomberg School of Public Health comprehensively reviewed the regulations on e-cigarettes in 123 countries.[48] Table 1 summarises the regulation and policies in Malaysia and the region based on literature review as well as web searches of government websites and media reports. Brunei, Singapore and Thailand have banned the sale of e-cigarettes; the jury is still out in Malaysia.

Table 1: Policies on sale of nicotine, tobacco products and e-cigarettes in different countries.

Country	Policy
Malaysia	The sale, distribution or importation of unlicensed *nicotine* containing e-cigarettes is prohibited and can only be sold by licensed pharmacies or registered medical practitioners. Devices *without nicotine* are classified as electrical appliances and is legal. Nicotine is classified as a Class C poison under the Poisons Act of 1952 and the Control of Drugs and Cosmetics Regulations of 1984 (Malaysia). Poisons Act forbids the sale or supply of poisons to people under 18. Liable to a fine not exceeding RM3,000 and / or up to two years imprisonment.
Australia[1]	Australian laws about e-cigarettes are complex and vary between different jurisdictions. • E-cigarettes containing nicotine cannot be sold in any Australian state or territory. • It is illegal to use nicotine in e-cigarettes without a prescription. • In Queensland it is legal to sell e-cigarettes that do not contain nicotine under the same conditions as for tobacco products.
Bahrain	E-cigarettes are classified as tobacco products. Bans of sale, importation and distribution. Tobacco control law prohibits the advertisement, promotion, sponsorship and use of tobacco products (including e-cigarettes) in enclosed public places and public transportation.
Brunei	E-cigarettes are tobacco imitation products. Tobacco Order prohibits the sale, offer for sale or importation of items that imitate tobacco products. Nicotine preparations above 7.5 percent are classified as poisons and the Poisons Act stipulates that a license/permit from the Pharmacy Enforcement Unit of the Ministry of Health must be obtained before a person can import, possess for sale or offer for sale any poison. Liable to a fine of $10,000.
Cambodia	Bans their sale, importation and use.
Hong Kong	E-cigarette containing nicotine is regarded as pharmaceutical product and must be registered with the Pharmacy and Poisons Board before sale or distribution. Prohibits the possession or sale of unregistered pharmaceutical product, and the possession or sale without authority of Part I poison. Liable to a fine not exceeding $100,000 and 2 years' imprisonment for each offence. Pharmacy and Poisons Ordinance (Chapter 138, Laws of Hong Kong).
Japan	Non-nicotine e-cigarettes are currently not being regulated. Nicotine e-cigarettes are classified as medicinal products. Japanese pharmaceutical affairs law - marketing approval for the sale, advertisement, manufacture, importation and distribution of medicinal products must be sought under this law. The Ministry of Health, Labor and Welfare permits the private importation of medicinal e-cigarettes for private use only and an amount of less than one month's supply.
Nepal	Bans advertising, promotion and sponsorship as well as use in public places and transportation.
New Zealand	Medicines Act states that e-cigarettes promoted as therapeutic products are classified as medicinal. As medicinal products, there are restrictions on sale, advertising and distribution. Smoke-free Environments Act prohibits the sale of nicotine-containing e-cigarettes. Non-nicotine e-cigarettes that are not marketed as therapeutic products can be sold, but not to minors under 18 if they look like tobacco products. E-cigarettes can be imported, provided they are for personal use only.
Philippines	E-cigarettes are classified as medicinal products and medical devices. They must pass the safety, efficacy and quality evaluation of the Food and Drug Authority of the Philippines for market authorization as a health product and health-related device to be issued. E-cigarettes are subject to clean air laws in the tobacco regulation act, which prohibits their use in public places and restricts their use on public transportation.

Country	Policy
Republic of Korea[52]	Nicotine-containing e-cigarettes are classified as tobacco products. Sale is banned to minors (under 19). Use is banned in public places and transport. Korea has the highest retail prices for e-cigarettes in the world under a special health tax (Tobacco Business Act). Electric cigarette possession among teenagers remains an issue.
Saudi Arabia	The sale and marketing of e-cigarettes is banned in accordance with a decision of health ministers of gulf countries.
Singapore[53]	Prohibits the import, distribution, sale or offer for sale of any article that is designed to resemble a tobacco product; that includes Vaporisers such as e-cigarettes, e-pipes, e-cigars and the likes. Liable to a fine not exceeding $5,000 for a first offence and a fine not exceeding $10,000 for a second or subsequent offence and any e-cigarettes imported will be seized and confiscated. Section 16 of the Tobacco (Control of Advertisement and Sales) Act. Tobacco (Control of Advertisements and Sale) Act (CHAPTER 309) (Original Enactment: Act 10 of 1993).
Thailand	Medicine Act prohibits manufacturing, sale and importation of "modern" medicinal products. Tobacco Products Control Act prohibits importation and sale of products imitating cigarettes. Notification by the Ministry of Commerce bans the import of e-cigarettes. Customs Acts prohibits people from bringing untaxed products into Thailand. There is no explicit law banning the use of e-cigarettes, but e-cigarettes are banned where laws prohibit smoking.
United Arab Emirates	Sale and marketing of e-cigarettes is banned in accordance with a decision of health ministers of gulf countries.
Vietnam	Classified as tobacco products. The national tobacco control law bans sale to minors and marketing/advertising. Smoking tobacco products is prohibited in public spaces and public transport, with the exception of designated smoking areas.

E-cigarettes are banned in Singapore and strict enforcement instituted. The public is encouraged to assist in identifying and reporting e-cigarette smokers, manufacturers and retailers. One peddler selling e-cigarettes was fined $64,500 by the Singapore Health Sciences Authority (HSA). All websites managed by the peddlers selling e-cigarettes were shut down.[49] There is no reason why Singapore's success in dealing with e-cigarettes cannot be repeated in Malaysia and the rest of the world, other than lack of political will. Whistle blowers can be rewarded from revenues generated from heavy fines, and punishment imposed on those who permit e-cigarette smoking on their premises, e-cigarette retailers, and smokers alike. The identity of whistle blowers should be protected, and whistle-blowing could provide a substantial income for many, and serve the public good.

Conclusion

There are no "health benefits" associated with e-cigarettes; it does not help stop or cure nicotine addiction; instead, it initiates and reinforces addictive behaviour. E-cigarettes should not be promoted as a means of getting tobacco smokers off their habit; nicotine patches are effective in this regards. Introduction of e-cigarettes only serves to increase the number of adolescents who have never previously smoked to be hooked on this addiction. Addiction in any form should not be supported. E-cigarettes should be banned despite fears that this may lead to a thriving illegitimate market promoted and supported by "Big Tobacco". The onus is on e-cigarette lobby to prove that e-cigarette is safe and not e-cigarette is safer than standard cigarette, and secondly, that e-cigarette does not increase nicotine addiction especially among adolescents and young adults.

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Family response to presume consent system on organ donation from a review of literature

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Background: Most countries around the world have experienced a shortage in organs needed for transplantation. Organ donation performance is widely attributed to two important factors: the legislation and the role of the family. Thus, this literature review aims to examine the willingness of people for organ donation while highlighting the importance of having a presumed consent system.

Methodology: In this study, we explored many papers of which 10 articles were studied to gain conclusive understanding of the two factors and their interactions.

Results: Our analysis of literature regarding the legislation and family response showed that the presumed consent system for organ donation accounted for 21 – 30% higher organ donation rates than the informed consent system. We also found a gap between the willingness of people to donate their own and their relatives' organs. The ratio of people willing to donate their organs after death was estimated to be 10 – 12% higher than the ratio of those willing to donate their relatives' organs. Furthermore, the study revealed the importance of a presumed consent system in raising the willingness of the people and their relatives for donation, but that did not eliminate the gap.

Conclusion: Countries seeking to overcome organ shortage and increase organ donation rates by moving towards the presumed consent system should consider the importance of providing families with proper information about this system. The fact that a gap between the willingness of the people to donate their own as well as their deceased relatives' organs exists, has to be conveyed to the governments, which will be helpful in optimising organ donation rates.

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Keywords: Family, informed consent, organ donation, presumed consent, public view

Introduction

Most countries around the world have experienced a shortage in organs needed for transplantation. However, some countries have succeeded in overcoming this problem while others are still lagging behind in terms of organ donation rates. The first step to solving this problem was cited as the change in the legislation of organ donation. Further, the role of the family in getting the expected results for such changes has been widely argued to be imperative.

The family has been considered as one of the most important factors affecting organ donation. The role of the family is crucial due to its implications on shaping an individual's personality and major life decisions. After one's death, the family replaces the individual's position regarding the decision making of their will and after death responsibilities. The last argument also applies for organ donation since various studies have found that a family played a vital role in determining the organ donation rates in most of the countries worldwide (Fevrier & Gay, 2004; Siminoff *et. al.*, 2001).

Social activities of individuals and families are believed to be affected by the organ-donation legislation. In this context, many studies have discussed the implications of those legislations on organ donation rates (Abadie & Gay, 2006; Fevrier & Gay, 2004; Siminoff *et. al.*, 2001). Although there is no consensus regarding the best legislation for optimisation of organ donation rates, most studies concluded that the presumed consent system resulted in higher organ donation rates than the informed one. These two systems were compared after controlling the other factors, such as education, religion, age, etc., which are believed to affect the organ donation rates (Abadie & Gay, 2006).

Based on the expected advantages of presumed consent over informed consent system and the successful experience of countries, some countries such as Spain, have shifted from the latter to the former system and

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have recorded higher organ donation performance. However, the experience of some countries have not been in favour of the presumed consent system proponents.

Given the vital role of both family and legislation in organ donation, the association between the legislation and organ donation rates can be explained by the role of the family (Rosenblum *et. al.*, 2012) as a mediator between the two. It is thus imperative to explore the literature regarding the response of families towards organ donation decision-making, within the framework of both legislations. Based on the results of the previous studies, a conclusive understanding of the mechanism of family, legislation and organ donation performance has been provided. Additionally, the comprehension of such mechanisms requires exploration of any difference between the family members' decision regarding the organ donation cases of their own and their loved ones, after death.

Thus, in this study, we focussed on exploring the literature pertaining to the following questions: (i) Does the family affect the relationship between the legislation and the resulting donation rates of this system? and (ii) Does the family members' response to organ donation differ when it comes to their deceased relative's organs rather than their own?

Methods

A limited number of studies have dealt directly with this issue. Therefore, we needed to explore many scholarly articles that investigated the matter to be able to present this literature study. For fulfilling this study purpose, we ran our search in different databases using the keyword "organ donation" combined with one or more of the following keywords: "family", "legislation", "presumed consent / opt-out", "informed consent / opt-in", ", and "family response". The search was mainly conducted in the following databases: Medline, Embase, PsycINFO, and ScienceDirect.

Our research found 1,335 articles pertaining to the subject matter of organ donations. After reviewing the titles and abstracts of these articles 1,250 papers were excluded as these papers were not directly relevant to the topic searched. The full text of the remaining 85 papers were analysed and only 10 papers were found relevant to the scope of this study. The 10 papers were selected as they were compatible with our inclusion criteria. We only chose (1) papers that discussed family responses towards organ donation, (2) papers that offer comparative analysis of countries, (3) and also those that are cited in the Publish or Perish software. Papers that chose to discuss apart from family response on organ donation or just focussed on the analysis of a particular country were excluded. Papers that were not cited in the Publish or Perish software were also excluded. The 1,335 papers were reduced to 85 on the basis that only papers that discussed about the presumed consent system were included. The papers were further reduced to just 10 by only including papers that discussed on family responses towards organ donation. This explains the reasons why a total of 1335 article was narrowed down to just 10 papers.

Before performing detailed analysis of family response and organ donation system, it was important to access and compare the findings of literature on the performance of organ donation systems in general. Hence, this study was structurally divided into three sections: (a) presumed consent versus informed consent systems; (b) legislation and family response; and (c) biasness in donation decision.

All human studies had been reviewed by the University of Malaya Research Ethics Committee (Reference Number: UM.TNC2/RC/H&E/UMREC-35) and have therefore been performed in accordance with the ethical standards laid down in an appropriate version of the 2013 Declaration of Helsinki as well as the Declaration of Istanbul 2008.

Results

(i) Presumed consent versus informed consent systems

Theoretically, the presumed consent system is believed to enhance organ donation rates. According to a recent survey (Rithalia, McDaid, Suekarran, Myers, & Sowden, 2009), the number of countries which adopted this system has rapidly increased; currently, 25 nations have applied this system officially. The proponents of the informed consent system are increasing in those countries who are unclear about the transition towards the presumed consent system. For instance, in the UK, the 2007 surveys revealed that around 60% of the respondents were in favour of replacing presumed consent with informed consent, compared to 20% in a survey done in 2000 (Mossialos, Costa-Font, & Rudisill, 2008).

In a review of 26 scholarly articles, five articles compared organ donation rates in different countries, before and after their shifting from an informed consent system to a presumed consent system (Rithalia *et. al.*, 2009). The authors concluded that countries that had shifted to the presumed consent system witnessed an increase in organ donation rates. Organ donation rates per million people (pmp) were recorded at an increased range between 21% and 30%. Eight of these studies were related to cross-country analysis, which revealed that the presumed consent system is responsible for increased organ donation rates compared to the informed consent system.

A cross national empirical analysis revealed that the legislation is one of the determinants of organ donation (Abadie & Gay, 2006). Their study showed that once the other determinants of organ donation were controlled, the presumed consent system appeared to record an average of 25 to 30% higher organ donation rates over the informed consent system.

The outcomes of studies within the European countries also supported the superiority of the presumed consent system over the informed consent system. A survey of 16,230 respondents from 15 European countries concluded that people are more likely to donate in the case of presumed consent system (Mossialos *et. al.*, 2008). Similarly, Gimbel *et. al.* (2003) found that the presumed consent system is one important factor for getting higher organ donation performance, besides other factors such as the number of transplant centres, education and religion.

In contrast, some other studies showed that the shift towards presumed consent may lead to negative outcomes. For instance, when Chile shifted towards the presumed consent system in 2010, the percentage of non-donors increased. The donation pmp decreased from 8.31 (mean of donation rates between 2000 and 2009) to 5.95 pmp (mean of donation rates between 2010 and 2011). Previously, Chile and Brazil had the same negative experiences, which urged the officials to abolish the presumed consent system in 1997.

(ii) Legislation and family response

In a recent study of legislations of 54 countries worldwide (25 countries with presumed consent and 29 countries with informed consent), Rosenblum *et. al.* (2012) found that in most of these countries, the deceased's families are involved in the organ donation process regardless of the consent system adopted. The study also showed that the family played an important role regardless of whether the deceased expressed a wish to donate organs.

In another study, Fevrier and Gay (2004) explored the role of the family in determining the relationship between the legislations and organ donation rates using mathematical models. The models were built based on the assumptions taken from the theoretical literature of organ donation decision and the utility theory arguments of cost and benefit. Initially, they proved that the presumed consent system resulted in higher organ donation rates than the informed consent system, without considering the role of family. However, after they included the role of family in the

model, the results were surprisingly new and a first of its kind in the field. They found that the informed consent system became more efficient than the presumed consent system in terms of organ donation rates. Results of this study opened new dimensions for scholars to rethink on the importance of including family response when explaining the interaction between the legislation and organ donation. However, real world data analysis of some studies were not in accordance with that the above argument.

Mossialos *et. al.* (2008) argued that the legislation system played an important role not only in people's preferences on donating their own organs but also their relatives' organs. Their study added that people from those countries with presumed consent system were more willing to give consent to donate their deceased relatives' organs compared to those countries with an informed consent system.

In contrast, the studies on Chile and Brazil concluded that the reluctance of families to give consent for organ procurement from their deceased relatives had increased after the countries applied the presumed consent system. However, these results were widely attributed to other reasons rather than the legislation only. The distrust towards medical systems and the absence of proper knowledge among the families regarding organ donation were cited as the main reasons for their reluctance to donate their own and their relative's organs. This explanation agreed partially with Mossialos *et. al.* (2008)'s findings, regarding the interaction of families with the legislation, where the interaction was found to affect organ donation significantly.

(iii) Biasness of the donation decision

Some of the reviewed studies investigated the differences between donation decisions of family members, regarding their own and deceased relatives' organs. The analysis of their findings showed that people are more willing to donate their organs rather than donating the organs of their deceased relatives.

In Belgium, where the presumed consent system has been applied since 1987, a study of three age groups was conducted: (i) young (18–29 years), (ii) parents (30–59 years) and (iii) grandparents (above 60 years) (Roels *et. al.*, 1997). The study revealed that 84.5, 83 and 60.2% of the three respective groups were willing to donate their organs. However, peoples' willingness to donate their relatives' organs was around 10% lower on an average; whereas only 72.3, 75.2, 54% were recorded for the three generations, respectively, stating their willingness to give consent regarding their deceased relatives' organs. The results from the Mossialos *et. al.*(2008)'s findings accorded with the notion. According to their outcomes, although 60.1% of people were willing to donate their organs, only 48.4% gave their consent for the procurement of organs of their deceived relatives. These findings implied that there is an approximate 10% gap of organs available for donation, which are lost due to the biasness in the preferences of people regarding their own and their relative's organs.

Table 1: Countries implementing presumed consent system for organ donation

Year	2010		2011		2012		2013	
Country	Deceased donor	Living donor	Deceased donor	Living donor	Deceased donor	Living donor	Deceased donor	Living donor
Austria	24.3	7.2	26.2	6.8	24.60	7.70	24.60	9
Belgium	25.2	6.9	29.3	7	32.9	8	29.9	9.6
Chile	5.4	0	6.61	0	9	0	6.43	0
Croatia	28.66	4.96	34.96	2.79	36.5	3	35	0.9
Hungary	15.80	4.19	13.08	4.69	14.32	5.30	15.61	4.03
Luxembourg	6.02	0	18	0	7.9	0	14.9	0
Singapore	5.10	7	0	6.11	0	5.4	0	0
Slovenia	20.5	0	15.5	0	23	0	24.30	0
Spain	32	5.53	35.30	7.20	34.80	8.20	35.12	8.59
Sweden	12.60	18.77	15.45	19.90	15.03	17.15	16	16.42

*Sourced from The International Registry in Organ Donation and Transplantation (IRODaT)
*Figures are presented in "PMP" form (per million of population)

Table 2: Countries implementing informed consent system for organ donation

Year	2010		2011		2012		2013	
Country	Deceased donor	Living donor	Deceased donor	Living donor	Deceased donor	Living donor	Deceased donor	Living donor
Australia	14	13.40	15.10	11.5	15.60	10.80	16.90	10.80
Brazil	9.60	9.10	10.70	9.17	12.60	8.40	13.2	7.90
Denmark	12.92	18.06	13.11	17.96	13.38	13.53	10.16	18.74
Germany	15.90	9.20	14.70	10.60	12.80	10.40	10.90	10.10
Ireland	9.70	0	20.67	6	17	7	18.81	8.31
Netherlands	13	28.80	13.23	27.10	15.08	29.32	15.26	31.24
Malaysia	0.7	1.30	NA	NA	0.64	1.84	0.5	1.87
Saudi Arabia	3.86	15.30	3.40	20.20	3.07	22.10	2.5	24.70
United Kingdom	16.40	16.90	17	17	18.34	16.86	20.77	17.80
United States	25.60	21.20	26	19.20	25.60	15.40	25.99	18.83

*Sourced from The International Registry in Organ Donation and Transplantation (IRODaT)
*Figures are presented in "PMP" form (per million of population)

The two tables indicate higher organ donation rates in many countries that have implemented the presumed consent system such as Belgium, Spain and Croatia, in contrast to the informed consent system. However, in Singapore and Chile, the organ donation rates have been dismal, even lower than some countries that implemented the informed consent system.

Discussion

While numerous campaigns and awareness programmes may have been carried out globally, organ donation rates remain dismal in most, if not all sovereign states. This is understandable because organ donation is more complex than one can imagine as it involves not only the consent of the possible donors, but also their immediate family members' approval. In the countries that have implemented the presumed consent system, the process of organ harvesting may become complicated if a deceased did not file any objection in his or her lifetime and the family members cite lack of information in filing such official objections in the past. The efforts taken through campaigns and awareness programmes may be dampened by disinterest or fear against organ donations caused by external factors. Such external factors may include the acts of corruption in handling the process of organ donation and transplantation or even unpleasant experiences of former organ donors. In the second half of 2012, Germany experienced a drastic plunge in organ donations from the deceased compared to the preceding year. This came about as corruption acts of doctors reporting their patients' health worse than it is in order to be placed as more urgent patients in the organ waiting list, were exposed. Apart from that, botched surgical procedures have also caused the donors not only health complications, but even death, although it has to be assured that such incidences remain very minor. Films, albeit aimed for entertainment, may also cause fear against organ donation. Examples such as "Recycled Parts" (2007) and "Kaaki Sattai" (2015 – Tamil film) portrayed "organ theft" from patients by doctors and unscrupulous syndicates, and may influence the audiences to reject organ donations in the future. On the same note, it is worth to be noted that films such as the block-buster flick "Seven Pounds" (2008), have encouraged the act of organ donation in the quest of saving lives.

Although the theoretical argument of Fevrier and Gay (2004) indicated a negative implication of family on organ donation rates, most of our reviewed studies, which were based on actual world data, concluded that the consent of the family for organ donation of their relatives was higher under the presumed consent system rather than the informed consent system. However, a few exceptions of this argument, such as the cases of Chile and Brazil, did not refute this argument but rather highlighted the importance of public trust and family education regarding the organ donation systems.

Our review showed that:

- Willingness of people to donate their organs after death was approximately 10 – 12% higher than their willingness to donate their relatives' organs. Further, the willingness in both the cases was higher under the presumed consent than the informed consent system.
- Most of the literature found, with some exceptions, the significant effect of legislations on organ donation and proved the effectiveness of presumed consent system in bringing the organ donation rates to 21 – 30% higher than the informed consent system.

Based on the information summarised in Tables 1 and 2, further studies on this area are highly warranted and can be used to understand the willingness towards organ donation among the population.

Conclusion

The isues highlighted in this study are the backbone of our suggestion that countries seeking to overcome organ shortage and increase organ donation rates by moving towards the presumed consent system should

consider the importance of providing families with proper information about this system. Furthermore, the fact that a gap between the willingness of the people to donate their own as well as their deceased relatives' organs exists, has to be conveyed to the governments, which will be helpful in optimising organ donation rates. This should be done by dedicating more studies to understand the reasons behind this gap and to suggest the possible solutions.

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Discordance between medication adherence and blood pressure control in primary care clinics in Negeri Sembilan, Malaysia: The problem of therapeutic inertia

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Introduction: Poor adherence to anti-hypertensive agents may be a major contributor for suboptimal blood pressure control among patients with hypertension. This study was conducted to assess the adherence to antihypertensive agents using Morisky Medication Adherence Scale (MMAS-8) among primary care patients, and to determine whether the blood pressure control is associated with the level of adherence.

Methodolgy: This cross-sectional study was conducted between June 2011 and August 2011. Adults with hypertension older or equal to aged 30 with or without diabetes were recruited from two public primary care clinics in Negeri Sembilan, Malaysia. Medication adherence was assessed using MMAS-8.

Results: Data from 231 patients were analysed, whereby 68% of them had good medication adherence but only 38.1% of the patients had their blood pressure under control. Statistical analysis failed to find correlation between adherence and blood pressure control. Twenty per cent of hypertensive subjects were on beta-blocker alone, and 37.1% of patients with either diabetes or proteinuria were not prescribed either angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blocker (ARB). Above half the patients (51.5%) were on monotherapy.

Conclusion: Discordance between adherence to anti-hypertensive agents and hypertension control is clearly shown in this study, and the likely explanation for the discordance is therapeutic inertia.

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Keywords: primary care, hypertension, therapeutic inertia, medication adherence

Introduction

Hypertension is a common co-morbidity amongst Malaysians and it has been on the rise. Among adults aged 30 years and above, the prevalence of hypertension has increased from 32.9% in 1996 to 40.5% in 2004.[1] Although the methodology used in this national survey may overestimate the true prevalence of hypertension[2], the rise of the disease is evident. Poorly controlled hypertension is a known major risk factor causing cardiovascular diseases like coronary heart disease, stroke, and congestive heart failure. Therefore, treating hypertension successfully is crucial in preventing, as well as curbing the rising health care costs associated with its complications. Unfortunately, among hypertensive patients who were on anti-hypertensive agents, only 26.8% had their hypertension controlled.[1] The failure of treatment has been largely attributed to non-adherence.[3-6]

Some authors defined adherence as "the extent to which a patient's behaviour (in terms of taking medications, following a diet, modifying habits or attending clinics) coincides with medical or health advice".[7-8] On the other hand, non-adherence is used in regard to a patient not taking a prescribed medication or following a prescribed course of therapy and constant negligence rather than just temporary forgetfulness or neglect of treatment. Patients who take 80% or more of their prescribed antihypertensive medications are considered adherent as it requires this amount of medication to produce a systemic reduction of blood pressure.[7]

Medication non-adherence is a serious and challenging issue concerning many healthcare providers. However, despite considerable effort to improve patient adherence, this continues to be a significant problem. It would be a waste of healthcare resources when medications are not taken appropriately or incorrectly. Furthermore, being non-adherent may impair patient's quality of life and make the condition more difficult to treat. It may even lead to further complications such as cardiovascular and renal diseases, and pose a financial strain to health management as well.

Medication adherence can be measured by chemical markers, surrogate reports, pill counting, electronic

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medication event monitoring system, patient self-report and prescription refill. Self-report measures of adherence have generally fared well in adherence measurement when comparing to other methods.[9] Eight-item- Morisky Medication Adherence Scale (MMAS-8) was developed in 2008. This scale has a reliability of 0.83 as well as good concurrent and predictive validity.[10] MMAS-8 has been widely used to assess medication adherence in other countries for different diseases. Malay version of MMAS-8 was validated by Al-Qazaz et al in their type 2 diabetes mellitus study.[11] The present study was conducted to assess the adherence to antihypertensive agents using MMAS-8 among primary care patients, and to determine whether the blood pressure control is associated with the level of adherence.

Methodology

This cross-sectional study received Ethics approval from International Medical University (IMU) Ethics Committee prior to data collection. Written informed consents were also obtained for all patients participating in this study.

Hypertensive adults were recruited by convenient sampling from the non-communicable disease clinics of two public primary care centres in Negeri Sembilan, Malaysia. Data was collected from the subjects between June 2011 and August 2011. The subjects were eligible if they have been followed up for at least a year at the clinics. All subjects were at least 30 years of age and had been prescribed with one or more antihypertensive medications.

The subjects were interviewed face-to-face prior to their consultation with their doctors using structured questionnaires. Patient compliance to antihypertensive drug therapy was assessed using the MMAS-8 (where appropriate using the English, Malay and Mandarin versions). The most recent three blood pressure readings of the subjects were extracted from their clinic records to explore the extent of blood pressure control.

SPSS version 19.0 was used for statistical analysis. Where appropriate we recorded continuous variable into categorical variables. MMAS-8 score, categorized as poor adherence (score <6) and good adherence (score ≥6)[7], was the dependent variable. Level of blood pressure control was based on Malaysian Clinical Practice Guidelines for the Management of Hypertension (2008) (i.e. good control was BP <140/90 for non-diabetic, and BP <130/80 for diabetic patients).[12] We compared independent and dependent variables using chi-square test. Independent variables that were associated with MMAS-8 score were entered into a logistic regression model. We determine linear relationship of three blood pressure readings using Pearson correlation. Statistical significance was set at $p<0.05$.

Results

Response rate

Of the 244 patients approached for this study, 12 patients refused to participate giving a response rate of 95.1%. One respondent did not complete the MMAS-8 and was excluded from the analysis. Total number of respondents available for analysis is 231.

Socio-demographic and lifestyle data

Table I shows the characteristics 231 study subjects, 98 of them also suffered from diabetes. Their mean age was 59 years (SD=10, age range 33 – 90 years). Smoking was reported by 28 subjects (12.1%), use of alternative medicine for blood pressure control by 34 subjects (19.7%), daily vegetable intake by 201 subjects (87.0%), daily fruit intake by 114 (49.4%), and 67 subject (29.0%) reported using home blood pressure monitor.

Table I: Socio-demographic correlates of good adherence

Characteristics	Number (%)	Good adherence	P value	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Gender					
Male	100 (43.3)	62.0%	0.090		
Female	131 (56.7)	72.5%			
Age Groups					
<60	119 (51.5)	58.8%	0.002	2.44 (1.37 to 4.33)	2.20 (1.19 to 4.09)
≥60	112 (48.5)	77.7%			
Ethnicity					
Malay	96 (41.6)	67.7%	0.655		
Chinese	64 (27.7)	65.6%			
Indian	68 (29.4)	69.1%			
Others	3 (1.3)	100%			
Education Level					
Secondary or more	109 (47.2)	59.0%	0.002	2.46 (1.38 to 4.39)	2.40 (1.32 to 4.39)
Primary or less	122 (52.8)	78.0%			
Employment Status					
Employed	72 (31.2)	54.2%	0.002	2.44 (1.36 to 4.37)	1.73 (0.92 to 3.25)
Unemployed / Retired	159 (68.8)	74.2%			

Blood pressure control, medication adherence and associated factors

The blood pressure (BP) of subjects, for both hypertension alone and hypertension with diabetes, is shown in Table II. Systolic blood pressure readings over the last three visits showed some correlation (r=0.31 to 0.40, p<0.05). Diastolic blood pressure readings over the last three visits showed moderate correlation (r=0.47 to 0.51, p<0.05). Slightly more than half of the patients with hypertension without diabetes achieved good blood pressure control (BP <140/90), while only 15% of subjects with hypertension and diabetes achieved good blood pressure control (BP <130/80). Overall, 38.1% of all hypertension subjects achieved good blood pressure control (Table III).

Patients' MMAS-8 scores ranged from 1-8 (median=6.75); 74 subjects (32.0%) had poor adherence, and 157 subjects (68%) had good adherence.

As shown in Table I, elderly subjects (aged ≥60), those with lower educational level (primary or less) and subjects who were unemployed or retired were shown to have better medication adherence in univariate analysis. In the logistic regression, only elderly and those with lower educational level were independently associated with good adherence.

We found that good blood pressure control was not associated with good adherence (Table III). We found also that only half of all study subjects received two or more antihypertensive agents. Blood pressure control and medication adherence were not associated with lifestyle

(smoking, daily fruit intake, daily vegetable intake), usage of home blood pressure monitor and consumption of alternative medicine (analysis not shown).

With regards to antihypertensive drug choices, we found that 20% of hypertensive subjects on monotherapy were prescribed beta-blocker alone. We also found that 37.8% of subjects with hypertension and diabetes were taking beta-blocker. Furthermore, 37.1% of hypertensive subjects who also have diabetes or proteinuria were not prescribed angiotensin-converting enzyme inhibitors or angiotensin receptor blocker.

Table II: Mean blood pressure level and prevalence of good blood pressure control

	Hypertension without diabetes	Hypertension with diabetes
Systolic blood pressure, mean in mm Hg (SD)	137 (17)	139 (16)
Diastolic blood pressure, mean in mm Hg (SD)	79 (10)	78 (9)
Good blood pressure control	73 (54.9%)	15 (15.3%)

Table III: Clinical factors and association with good adherence (n=231)

Characteristics	Number (%)	Good adherence (%)	P value
Blood pressure controlled			
Yes	88 (38.1)	64.8%	0.415
No	143 (61.9)	69.9%	
Number of medication			
1 only	119 (51.5)	66.0%	0.576
≥2	112 (48.5)	69.5%	

Discussion

In our study, two thirds (157/ 231) of the patients had good adherence rate, which is consistent with the studies conducted by Morisky *et al*[10] and Lee *et al.*[13] However, a study conducted by Ramli et al in Selangor, using self-developed questionnaire recorded 53.4% of good adherence rate.[14] The difference in adherence rates between the two studies may be due to the different questionnaires used or locality. The adherence rate could also vary with different setting, locality or methods used. Using pill count method, Lim *et al*[6] and Aziz *et al*[3] recorded good adherence rate of 74% and 44% respectively. Nonetheless, a self-reported measure of adherence is more reliable compared with other methods.[9]

It is commonly believed that elderly and less educated patients are less compliant to medications; however, our study has shown the reverse that elderly and those with lower educational level were independently associated with of good adherence. It is thought that as a person's age advances, one would be more careful or concerned about their health status. A study done by Weingarten et al showed that age is an important factor in determining adherence, whereby they noted patients under the age of 55 years or over 65 years had significantly lower adherence than those aged 55 – 64 years.[15] Since the mean age of our patients is 59, this could partially explain the high adherence rate seen in our study.

Another variable which could have contributed to the adherence rate is the level of education the study subjects has achieved. The results of our study show that those who have an education background up to primary school level have the highest percentage (53.8%) of adherence levels. This finding is consistent with the finding of Larsen *et al*, that those with a shorter duration of education (duration of 0 to 6 years, which is equivalent to the number of years to complete primary education level in Malaysia) recorded a significantly high adherence level.[16]

One would expect that high adherence rate should be accompanied by high percentage of blood pressure control among patients. However, our study did not show an association between the level of adherence and blood pressure control. In fact, in two thirds of patients with good adherence rate, only 38.1% of hypertensive patients with or without diabetes had their blood pressure under control. This finding is in contrast to previous studies.[10, 13] The lack of association between level of adherence and blood pressure control in our study could be secondary to therapeutic inertia. Therapeutic inertia, also known as clinical inertia, is defined as "failure of health care providers to initiate or intensify therapy when indicated".[17] This phenomenon is estimated to be present in more than two thirds of population with uncontrolled hypertension.[18] In the present study, we found that 20% of hypertensive subjects were on beta-blockers alone, and 37.1% of the patients with either diabetes or proteinuria were not prescribed either angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB). These findings reflect poor adherence of physicians to guidelines and problem of therapeutic inertia. The poor adherence of physicians to guidelines is most likely due to the lack of education, training, and practice organization aimed at achieving therapeutic goal.[17] The other reason contributing to therapeutic inertia is that physicians fail to intensify antihypertensive treatment when targets are not achieved, as many feel that a clear improvement in BP without reaching the goal is acceptable and that the full drug effect may take up to several weeks to be reached.[19]

As subjects were recruited during their doctor visits, only those who came in for visits could be selected. Patients who defaulted on their follow-ups are likely to be non-compliant to medical advice and treatment plan. This group of patients was not included in the study. Such selection bias may falsely increase the percentage of patients with good adherence.

Discordance between adherence to anti-hypertensive and hypertension control is clearly shown in this study, and the likely explanation for the discordance is therapeutic inertia. As shown in many studies, therapeutic inertia is a major factor that hinders the control of hypertension; therefore more studies need to be conducted locally to explore ways to overcome this problem.

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Is Google search a useful medical diagnostic tool for third year medical students?

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Introduction: In recent years, the internet has become an increasingly popular tool for people to obtain information due to the overwhelming availability of material. As internet access becomes more readily available, the newer generation of patients, medical students and doctors are starting to prefer the internet as a source of reference to acquire medical knowledge. The main objectives of this study were to determine the accuracy of using Google search in establishing a clinical diagnosis based on information provided from the New England Journal of Medicine (NEJM) and to determine the concordance rate of Google diagnosis with the actual diagnosis from NEJM.

Method: The research design was a cross sectional study of 200 NEJM cases. The research team comprised of four 3rd year medical students and one senior supervisor. Google search engine was used to obtain a diagnosis. The time allocated for a Google search for each case was 20 minutes regardless of the number of websites used. The top two diagnoses were then compared to the actual diagnoses of the NEJM case and the accuracy of Google was then assessed.

Results: The study achieved a congruence of 71.5%. This is considered acceptable and satisfactory as the cases presented in NEJM covered a wide variety of problems and encompassed rare diseases.

Conclusion: From the final results obtained, it can be concluded that with the aid of Google, medical students in their 3rd year of their Bachelor of Medicine and Bachelor of Surgery programme are able to obtain a reasonable clinical diagnosis.

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Keywords: Google search, diagnosis, clinical case, congruency

Introduction

The internet has become an integral part of our daily lives and has risen to be the most convenient source for seeking information.[1,2,3] Its value as a learning aid is well recognised. As access to the internet has become more readily available, it has assisted doctors and medical students in their zest for exploratory approach to acquisition of knowledge. 'Google' is currently ranked as the most widely used search engine worldwide and remains a very popular choice for the simple reason that it is a freely accessible, user friendly search engine offering a breadth of endless amount of information.[4,5]

Although 'Google' is not primarily known to be a medical search engine, healthcare professionals, medical students and patients use it frequently for internet search related to illnesses and health. One of the main disadvantages of internet search is credibility of information raising questions as to its correctness and reliability.

To improve accuracy of information, reliable sources posted in the websites should be used. For example, to obtain information on medical health and illnesses, the New England Journal of Medicine, Lancet and British Medical Journal have continuously updated articles on a wide variety of medical diseases with thorough explanations, all available at the click of a computer mouse. These journals are reputed to contain consistent and trustworthy information for healthcare professionals.

With the Y-generation of medical students being technology dependent and competent, using the internet to obtain information seems to be the more popular choice compared to traditional library books. In order to be aware of the latest updates in the medical field, the internet also seems to be a better choice as information is continuously updated unlike published textbooks that contain information almost five to ten years old.

The main objectives of this study were to determine if 3rd year clinical (medical) students were able to use layman 'Google' search engine (www.google.com) to establish a clinical diagnosis based on cases derived from Massachusetts General Hospital case reports obtained from the New England Journal of Medicine (NEJM)

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and to determine the concordance rate with established diagnoses. This followed a preliminary study by the lead author on a smaller sample, the results of which were published elsewhere in 2010.[6]

Materials and Methods

The study design is shown in Figure I. The sample size consisted of 200 consecutive Case Records of the Massachusetts General Hospital obtained from the New England Journal of Medicine (NEJM) from years 2001 to 2009. Each case was summarised by a pair of 3rd year medical students who were in semester 6.

The four medical students who were assigned to the lead author to perform their research project were paired to work on 100 cases each under the supervision of the senior author. They were paired off so that two students could summarise selected cases while the other pair performed the 'google search'. Summary of each case highlighted the key clinical features without providing the diagnosis, keeping anonymous the NEJM case number or year of publication.

Group A (Figure I) initially summarised 100 cases while Group B was expected to solely use www.google.com search to arrive at the most likely diagnosis by entering important keywords from the summarised case. The time allocated for each case was limited to 20 minutes regardless of the number of websites used. The students were only to access www.google.com without accessing advanced searches like google scholar.

After the completion of 100 cases, roles were switched between the two groups for the remainder 100 NEJM cases. Separation into two groups (Groups A and B) was to eliminate bias towards the search result and to allow each pair the opportunity to learn skills in summarising and establishing a clinical diagnosis.

Cases were then sorted according to their difficulty viz. "EASY", "AVERAGE" and "DIFFICULT". The cases labeled "EASY" involved a recurrent problem, relapse of a similar problem, the diagnosis being revealed through obvious investigations (e.g. gene study, blood culture, antigen-antibody result, tissue biopsy, endoscopy etc.), characteristic signs and symptoms for the problem and problems associated with strong familial link. The case would be considered "AVERAGE" if it had sufficient investigations leading to the diagnosis and suggestive signs and symptoms although not characteristic of the final diagnosis. Lastly, "DIFFICULT" was assigned to cases where the presenting signs, symptoms and investigations were incompletely linked to the final diagnosis, a rare problem seen in other countries, vague and uncommon presentation as well as signs and symptoms suggestive of more than one problem hence complicating the diagnosis (Table I).

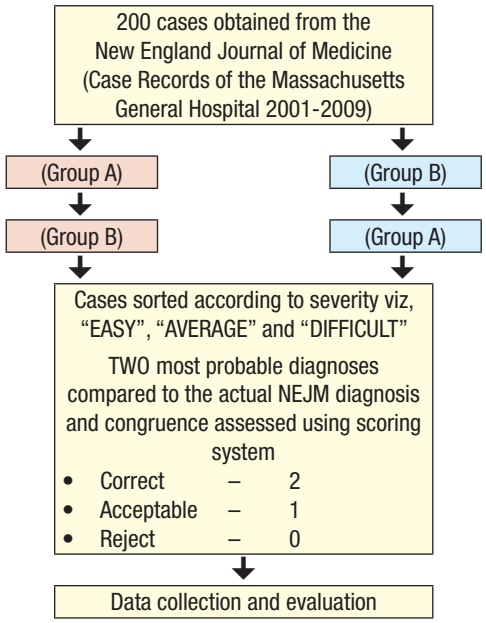

Figure I: Study Design

Table I: Scoring System

Google Diagnosis	Score
Correct	2
Acceptable	1
Rejected	0

At the end of the study, under the guidance of the lead author, both groups met to determine diagnoses that were correct, acceptable or rejected as compared to the actual NEJM diagnosis using a scoring system as shown in Table II. A total score of both diagnoses made by the pair of students amounting to 1 or higher would indicate a positive concordance rate ("YES") while a score of 0 (i.e. both diagnoses were rejected) would indicate a negative concordance rate ("NO"). Statistical analysis was done using a statistical analysis software, SPSS Version 11.5.

Chi square test was used to determine significance of differences in performance between Groups A and B.

Table II: Examples of categorisation of cases by difficulty and scoring

Case No / Year	Category of Difficulty	NEJM Actual Diagnosis	"Google Diagnosis'	Score assigned	Concordance
Case 34 – 2001	Easy – recurrent problem	Subcutaneous panniculitis-like T-cell lymphoma of γ/δ T-cell derivation.	1. Recurrent panniculitis	2	YES
			2. Erythema Induratum	0	
Case 1 – 2002	Easy – organism given	Infection with Loa loa	1. Schistosomiasis	2	YES
			2. Milroy disease	0	
Case 4 – 2002	Average – similar presentation	Glomerulonephritis mediated by anti-glomerular-basement-membrane antibodies.	1. Acute kidney failure secondary to bacterial sepsis	0	YES
			2. Acute nephritic syndrome secondary to infective endocarditis	1	
Case 19 – 2003	Difficult – pediatric case	Transient myeloproliferative disorder with trisomy 21 mosaicism	1. Neonatal Herpes Simplex virus infection	0	NO
			2. Transient Neonatal Pustular Melanosis	0	
Case 7 – 2003	Difficult – uncommon	Pneumococcal sepsis with endocarditis Endogenous endophthalmitis due to metastatic infection with Streptococcus pneumoniae.	1. Optic neuritis secondary to respiratory infection (Streptococcus pneumonia)	0	NO
			2. Bacterial keratitis secondary to respiratory infection (Strep pneumonia)	0	

Results

The concordance of NEJM diagnosis with diagnosis made from Google search obtained by Group A and Group B is shown in Figure II. Group A achieved 72% congruence whereas Group B obtained 71% congruence from 100 NEJM cases. With chi-squared value of 0.025 and degree of freedom of 1, p -value 0.876, there is no difference in performance between the two groups.

This showed that students were mostly able to make at least one acceptable diagnosis for most of the cases. One hundred and forty three (71.5%) scored one and above while 57 (28.5%) scored zero. The crude congruence rate was 71.5%.

Sub-analysis of the results was done by sorting the 200 cases into "EASY", "AVERAGE" and "DIFFICULT" (Figure II). There was an obvious downward trend in the congruence rate with increasing complexity of the cases. Among the "EASY" cases congruence rate of 99% (95/96) was obtained, whereas among "AVERAGE" it was 71.7% (38/53). Of the 51 "DIFFICULT" cases, students could only achieve a congruence of 19.6% (10/51). There was a large difference of 79.4% in the congruence rate between "EASY" and "DIFFICULT" NEJM cases.

Elimination of 96 "EASY" cases resulted in reduction of the total number of cases to 104, showing a corrected congruence rate of 41.2%.

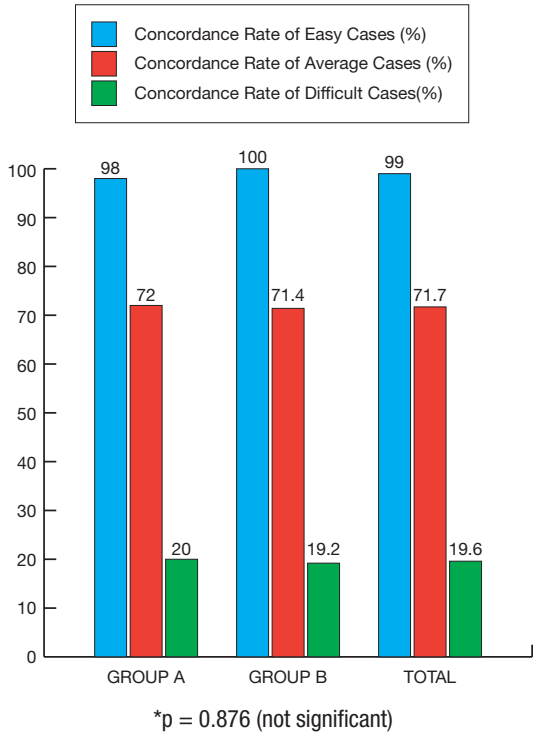

Figure II: Concordance rate by difficulty

Discussion

Medical training today encourages knowledge gathering and data mining using the internet. While medical students are provided skills learning and fundamentals of basic science in their formative years, they need to go through contextual learning in the clinical field to enable them to apply knowledge to practice.

This study of 200 Case Records from Massachusetts General Hospital initially had a crude congruency rate of 71.5%, with a corrected congruency rate of 46% after elimination of "EASY" cases. This is similar to a previous study done by the senior author (Nalliah S) using a smaller sample of 47 cases (concordance of 44.7%) without categorisation by difficulty.[6] Other factors contributing to the minor difference in congruence rate between the two studies are the different sample sizes, number of students involved, type of cases selected from NEJM and the length of time spent on each case. A pioneering study by Tang & Ng in 2006 using Google as a diagnostic aid with a sample size of 25 NEJM cases obtained a congruency rate of 57.7%.[7] In that study physicians were involved in internet search.

A difference of 25.5% from initial and corrected congruence is due to the fact that majority of the cases that were concordant and correctly diagnosed were "EASY" cases. Most "EASY" cases (89 / 200) had a total score of two, six cases had a score of three and two cases had a perfect score of four.

This is firstly attributed to the ease of availability of medical information on the internet combined with cognitive skills of third year medical students. Secondly, there were several NEJM cases which had very typical symptoms which were specific for certain diseases. Furthermore, there were some cases in which the patient had underlying disorders which led students to think that the current symptoms could be due to a manifestation of those disorders and other cases in which there was an obvious diagnosis from a history of a chronic, recurrent problem.

These results could be due to the value of medical training in the first three years of the MBBS programme that permits students to apply basic science in pathology to clinical medicine.

There were 57/200 NEJM cases with a score of zero indicating both diagnoses made by each student were wrong. This was due to the complexity and unfamiliarity of certain cases that required knowledge and skills that had yet to be developed by a third year medical students who had only completed three hospital postings (rotations) namely, internal medicine, general surgery and family medicine. They had not been exposed to other specialised disciplines like O&G and Paediatrics. Fifteen out of 200 NEJM cases were from Paediatrics and students were unable to come up with a diagnosis in four of those cases.

Among the difficult cases, there were ambiguous clinical symptoms where students were unsure of the diagnosis. A concordance rate of about 19.6% for the difficult cases is commendable considering the complexity of cases in NEJM and unfamiliarity of cases as they are derived from hospitals in USA.

Increasing the sample size to 200 permitted a cross over between groups so as permit evaluation of Google search skills of all the four students. There was no significant difference in the performance of both groups alluding to similar traits and levels of clinical competence in problem solving and establishing a clinical diagnosis.

Limitations:

Several limitations were identified throughout the course of the study. As the four medical students were only in their third year of their MBBS programme there was some deficit in knowledge and clinical ability to diagnose cases that required added knowledge. There was no dedicated research time allocated for the study within the MBBS course, hence students were expected to do the research concurrently with ongoing clinical rotations. All four students were in different clinical rotations. This made meet-ups for discussion and brain storming more difficult. Nevertheless, a weekly update on the progress of the study was done to ensure all students and mentor were aware of the progress. However, one of the strengths from this study was that the four students learnt the importance of group interaction and communication skills when working in a group.

Conclusion

There is a crude congruence of 71.5% for the total of 200 NEJM cases. Using a larger sample size with the possibility of cross-over of subjects resulted in higher crude congruency rate compared to a previous study by the lead author (44.7%; n= 47 NEJM cases). Differentiating the cases according to severity and eliminating "EASY" cases, a congruence rate of 46% was achieved for a total of 104 NEJM cases. This produced a narrower difference in congruence to the aforementioned study. This study also proved that, given fundamental clinical contextual learning in the 3rd year of the MBBS programme and a strong foundation in basic sciences, students are able to perform problem solving even for complex cases with the assistance of Google search. The research further concludes that there is no significant difference between the knowledge of 3rd year medical students who are in the first year of the clinical phase in the MBBS programme. Furthermore, this research establishes that with the easy availability of information online together with a reasonable level of cognitive skills, Google is a valuable tool to aid and guide medical professionals in clinical problem solving.

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Factors deterring registered nurses from pursuing post graduate nursing degree in a private hospital in Penang, Malaysia

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Background: In Malaysia the percentage of diploma registered nurses outnumber the percentage of degree registered nurses. Internationally, most registered nurses earn associate degrees or bachelor's degrees in nursing. Malaysia is in the pipeline of ensuring that its registered nurses are professionally qualified with nursing degree by year 2020. Registered nurses with diploma qualification are feeling the pressure to upgrade their qualification to degree. There are concerns as to why these nurses are not pursuing their post registration nursing degree.

Objective: To determine factors that are deterring the registered nurses of a private hospital in Penang from pursuing the post registered nursing degree.

Methods: This descriptive study utilised a convenient sample of 150 registered nurses from Lam Wah Ee Hospital in Penang. The instrument of this study was developed based on literature search and the conceptual framework of Force Fields Analysis developed by Kurt Lewin in 1952.

Results: The deterring factors for registered nurses not pursuing post registration nursing degree from this hospital were determined through negative mean score, which was valued at less than 2.5. The top 3 deterring factors identified were: high educational cost, with a score of 1.92; financial commitment, with a score of 2.22 and time constraints and high workload, with a score of 2.27.

Conclusions: High educational cost, financial commitment, time constraint and high workload were the main factors deterring the registered nurses from this hospital from pursuing their post registration nursing degree. Thus it is timely for the organisational management to consider workable measures to assist and motivate their nurses to upgrade themselves with nursing degree in line with Malaysia's vision to meet the increasing challenges and complex needs in the care of clients in health services.

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Key words: bachelor degree in nursing; continuing education; nursing education; Malaysian nurses.

Introduction

The post registration nursing degree programme or nursing baccalaureate programme offers a great range of field of studies which include nursing science, physical science, research, management, social science, humanities and public health (Soon, n.d.). Upgrading oneself to this educational level opens the pathway for registered nurses (RNs) to cope with current demands and workloads in managing the care of clients. The Institute of Medicine (IOM) report (2010) mentioned that the demand of 80% of baccalaureate-prepared nurses by 2020 is crucial to meet the higher and greater complexities in healthcare. The Ministry of Higher Education and Ministry of Health Malaysia are strategising to ensure that at least 60% of the nurses' population in this country possess a professional degree in nursing in order to meet the needs for clients care by 2020 (Hamidah Hassan, 2010).

Malaysia has an estimated 90% of diploma holder RNs and 10% of degree holder RNs in year 2012 (Lim, 2012). Based on the results of a local research done on 792 participants in 2013, 76% of the RNs were diploma holder, a small percentage of only 2.3% of RNs had degree and there were no Master or PhD holder among these groups of participants (Chong, Francis, Cooper & Abdullah, 2014). The low percentage in RNs with degree is also evidenced among the population of the RNs from this study site.

Factors deterring RNs from pursuing post registration nursing degree range from time constraints, geographical barrier, work and family responsibilities with childbearing duties, financial concerns and lack of differential treatment between associate-degree prepared RNs and baccalaureate degree-prepared RNs by employers. (Cathro, 2011; Lim, 2012 & Schwarz, 2014). Age and years of experience in nursing were

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found to be positively correlated to the deterring factors (Nash, 2013). The tendency for RNs with many years of working experience in nursing to further their education would be less as it was deemed stressful for them after staying off from studying for some time (Cathro, 2011; Nash, 2013 & Romp *et al.*, 2014). It was acknowledged that RNs were also challenged with time to study and to complete their assignments due to the frequencies of having to work double shifts / overtime (Lim, 2012).

Nurse Managers should provide more opportunities and recognition towards the nursing degree in order to encourage more RNs to upgrade themselves (Chiu, 2005). Many RNs are reluctant to pursue a degree programme due to lack of support from their organisation (Nash, 2013). Educational grant or sponsorship, study leave and time off would be an encouragement for more RNs to study nursing degree (Lim, 2012). Cathro (2011) and Nash (2013) agreed that a flexible working schedule would allow RNs to pursue a nursing degree programme.

The objective of this study was to determine the factors that deter the RNs from pursuing their post registration nursing degree in Lam Wah Ee Hospital in Penang, Malaysia. The result from this study was important to provide the needed insight to the hospital administrators of this hospital to increase the numbers of RNs with degree in line with the national strategy by year 2020. This hospital is still far from meeting this strategy as the numbers of RNs with degree holder were only 67 out of a total of 271 RNs with diploma qualification.

Methodology

A quantitative descriptive research design with convenient sampling technique was used for this study. In this sampling technique the authors focussed on RNs who were available and willing to participate and they must meet the inclusion criteria of this study. Convenient sampling provides a fast and the least expensive technique of sampling (Burns & Grove, 2009) within a limited timeframe of study. The inclusive criteria were: RNs with a minimum or more than 3 years of working experience that had done, or not yet or still undergoing their post registration nursing degree. Exclusive criteria were RNs who were temporarily employed or under probation period, those with less than 3 years of working experience and the RNs with administrator role of Sister and Matron. The sample size for this study was determined by simplified formula for proportion calculation (Yamane, 1967) with confidence level of 95%, degree of variability (p = 0.5) and level of precision (e = 0.05) from population size (N) of 233. With an added attrition rate of 10%, the calculated sample required was 162.

The research variable of this study was "deterring factors of RNs of a private hospital in Penang pursuing post registration nursing degree". Deterring factors were conceptualised as circumstances, facts or influences that discourage or prevent someone from doing something (Oxford dictionaries, 2014). There were 8 main attributes categorised for measurement under deterring factors. They were lack of personal interest or career advancement, career requirement, high educational cost, financial commitment, family commitment and support, time constraint and high workload, lack of support and motivation from superior or organisation and lack of flexible learning programme. The attributes were measured by a self-reported survey questionnaire formulated based on the conceptual framework of Force Fields Analysis developed by Kurt Lewin in 1952 and literature search. A four-point Likert rating scale was used for the questions, where the participants could either: strongly disagree = 1, disagree = 2, agree = 3 and strongly agree = 4. Informed consent and study information sheets were included with each set of the questionnaire. A pilot study was conducted on 15 RNs (10% distribution of the population) from a selected ward in the studied hospital (these RNs were excluded from the actual study). The RNs were asked to identify any items they had difficulty in answering and to specify the length of time it took for them to complete the questionnaire. Internal consistency test by Cronbach Alpha yielded a score of 0.88. As the pilot

study's participants were less than 25 (Hertzog, 2008), the Cronbach Alpha test was computed on the 150 actual RNs responses, which resulted in a good internal consistency of 0.80 to 0.91 for the eight subscales. Content validity for each of the items from the questionnaire was reviewed by 7 panels of experts from the selected private hospital to evaluate the suitability of questions posed. The items content validity index was from 0.8 to 1.0. The items-level content validity index should be not lower than 0.78 (Lynn, 1986).

In the actual study, informed consent and study information sheets were included with the questionnaire placed into a sealed envelope and distributed to units and departments of the hospital. The RNs were given a duration of one month, from 28th November till 28th December 2014, to fill up the questionnaires. The aim was to provide ample time for the RNs to reflect and answer the questions posed taking into consideration they were busy working with double shifts / overtime. This leniency also allowed the authors to obtain optimum return of questionnaires. Available and willing participants were instructed to return their informed consent and answered questionnaires in a sealed envelope into the designated drop box at various identified locations. This study was approved by IMU Joint-Committee on Research and Ethics.

The data collected was analysed using Predictive Analytics Software (PASW) in frequencies, percentages and mean scores.

Results

The response rate for this study was 92%. There were 159 returned questionnaires; however only 150 respondents had answered all the questions in full. The demographic data of the 150 respondents were tabulated in Table 1 below.

Table 1: Demographic data of respondents. (n = 150)

Characteristic	n	%
Age (yr)		
< 26	42	28.0
26 – 30	72	48-0
31 – 35	20	13.3
36 – 40	8	5.3
41 – 45	5	3.3
> 45	3	2.0
Marital status		
Single	86	57.3
Married	64	42.7
Number of children		
Nil	101	67.3
1	15	10.0
2	25	16.7
3	8	5.3
4	1	.7
Year of working experiences in nursing		
3 – 7	105	70.0
8 – 12	27	18.0
13 – 17	14	9.3
>17	4	2.7

Characteristic	n	%
Current educational level		
Diploma in Nursing	77	51.3
Post Basic Course	61	40.7
Degree in Nursing	7	4.7
Degree in Nursing & Post Basic Course	1	3.3
Basic Salary Scale		
RM 1500 – RM 2000	52	34.7
RM 2100 – RM 2500	50	33.3
RM 2600 – RM 3000	29	19.3
> RM 3000	19	12.7
Departmental Shift Pattern		
3 shifts	38	25.3
12 hours shift	84	56.0
Office Hours	14	9.3
Others	14	9.3

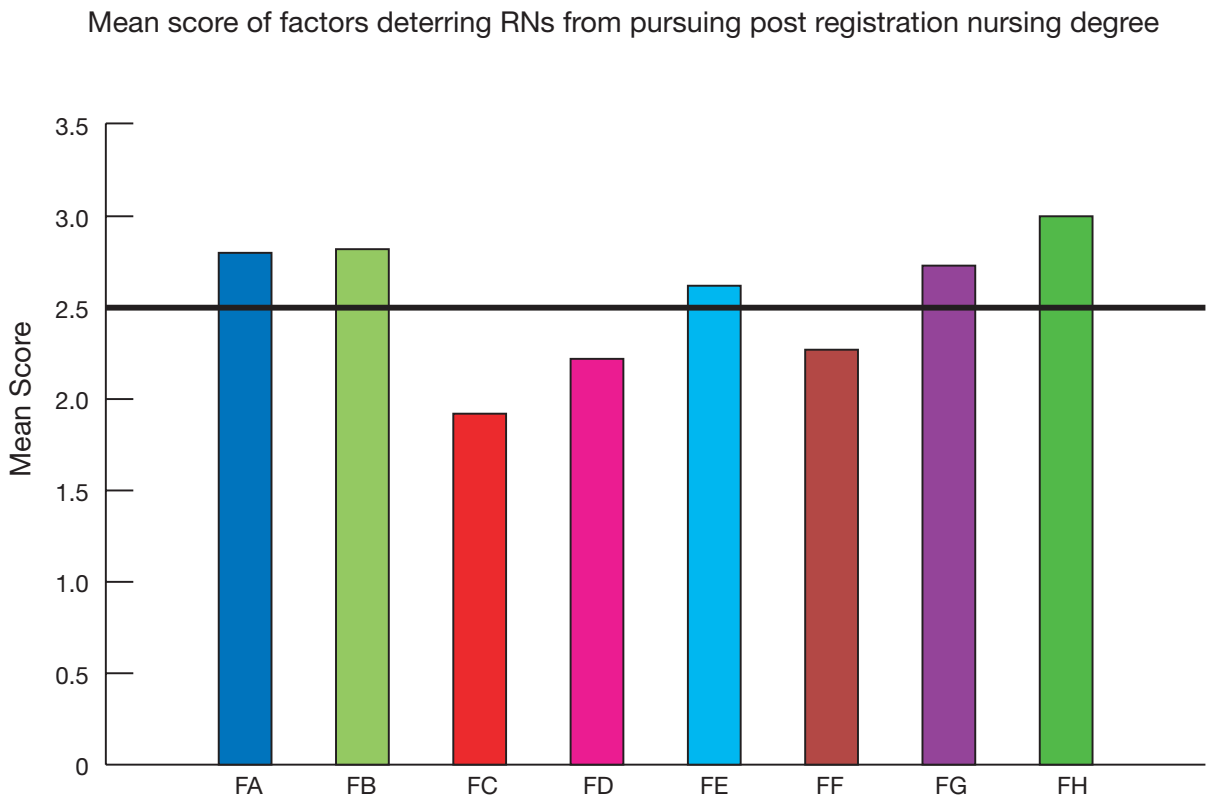
Table 2: Mean scores of demographic data according to the factors of Lack of Personal Interest or Career Advancement, Lack Career Requirement, High education Cost, Financial Commitment, Family Commitment & Support, Time Constraint & High Workload, Lack of Support & Motivation of Superior/Health Organisation, and Lack of Flexibility of Programme (n=150).

Deterring / Factors Demographic Data	Lack of Personal Interest or Career Advancement	Career Requirement	High Educational Cost	Financial Commitment	Family Commitment & Support	Time Constraint & High Workload	Lack of Support & Motivation from Superior / Health Organisation	Lack of Flexibility of Programme
Age								
< 26	2.72	2.82	1.89	2.27	2.68	2.16	2.58	3.00
26 – 30	2.80	2.82	1.94	2.30	2.73	2.28	2.28	3.01
31 – 35	2.92	2.78	1.82	1.96	2.25	2.28	2.26	2.95
36 – 40	2.88	3.16	1.88	1.97	2.13	2.21	2.69	2.81
41 – 45	2.96	2.60	2.40	2.30	2.47	2.60	2.53	2.95
> 45	3.00	2.67	1.67	2.00	2.89	3.00	2.72	3.33
Marital Status								
Married	2.77	2.83	1.91	2.23	2.80	2.21	2.69	3.00
Single	2.84	2.79	1.92	2.12	2.37	2.34	2.80	2.99
Number of Children								
Nil	2.80	2.83	1.90	2.30	2.76	2.24	2.69	3.02
1	2.83	2.70	2.03	2.02	2.49	2.31	2.82	3.02
2	2.82	2.92	1.96	2.13	2.29	2.35	2.82	3.01
3	2.83	2.56	1.94	1.97	2.13	2.33	2.67	2.75
4	2.60	3.25	1.00	1.50	2.00	1.67	3.50	2.75

Deterring / Factors Demographic Data	Lack of Personal Interest or Career Advancement	Career Requirement	High Educational Cost	Financial Commitment	Family Commitment & Support	Time Constraint & High Workload	Lack of Support & Motivation from Superior / Health Organisation	Lack of Flexibility of Programme
Years of Working Experience								
3 – 7	2.76	2.82	1.99	2.28	2.73	2.22	2.70	3.01
8 – 12	2.89	2.77	1.87	2.11	2.36	2.33	2.90	3.03
13 – 17	2.89	2.93	2.07	2.05	2.28	2.19	2.65	2.82
>17	2.95	2.69	1.88	2.06	2.58	3.17	2.58	3.19
Current Educational Level in Nursing								
Diploma in Nursing	2.74	2.76	1.89	2.27	2.63	2.12	2.70	2.98
Post Basic Course	2.84	2.84	1.94	2.16	2.58	2.15	2.74	2.98
Degree in Nursing	3.14	3.14	2.00	2.11	2.71	2.43	2.98	3.12
Degree in Nursing & Post Basic Course	2.88	3.00	2.00	2.35	2.67	2.73	2.77	3.15
Basic Salary Scale								
RM 1500 – RM 2000	2.68	2.80	1.83	2.67	2.68	2.19	2.68	3.01
RM 2100 – RM 2500	2.86	2.82	2.00	2.26	2.68	2.27	2.75	3.01
RM 2600 – RM 3000	2.86	2.90	1.97	2.22	2.54	2.28	2.86	2.97
>RM 3000	2.92	2.76	1.89	2.00	2.39	2.46	2.64	2.97
Departmental Shift Pattern								
3 shifts per day	2.85	2.85	1.92	2.35	2.80	2.17	2.74	3.04
12 hours shift	2.79	2.75	1.98	2.17	2.59	2.32	2.73	3.00
Office Hours	2.83	3.11	1.68	2.14	2.38	2.40	2.74	2.95
Others	2.71	2.86	1.79	2.23	2.50	2.10	2.71	3.00

Table 2 shows the overall mean scores of demographic data according to the 8 factors deterring the RNs from pursuing their post registration nursing degree. Comparison of findings for marital status according to family commitment showed that the respondents who were single had positive mean score of 2.79 while married respondents had negative mean score of 2.38. Comparing marital status to the number of children, those married respondents with 4 children had lower mean scores then those married but without children. Comparing the mean scores on years of working experiences to personal interest or career advancement, respondents with working experiences of 17 years and above in nursing had the highest mean score of 2.95. The respondents' basic salary scale which was more than RM 3000 had the lowest mean score of 2.00 when comparing financial commitment. All the departmental shift patterns showed negative mean scores in the comparison with time constraints and high workload.

Figure 1. Overall mean score of factors deterring RNs from pursuing post registration nursing degree.



FA : Lack of personal interest or career advancement
FB : Career requirement
FC : High educational cost
FD : Financial commitment
FE : Family commitment and support
FF : Time constraint and high workload
FG : Lack of support and motivation from superior or health organisation
FH : Lack of flexible learning programme

The mean scores of 8 the factors which deterred the RNs from pursuing the post registration programme are shown in Figure 1. The mean scores identified for deterring factors were less than 2.5. Mean score for high educational cost was 1.92, financial commitment's mean score was 2.22 and mean score for time constraints and high workload was 2.27. They were identified as the top 3 factors that were deterring the respondents in this study from pursuing their post registration nursing degree.

Discussion

The majority of the respondents from this study echoed that offering study opportunities, staff promotion, empowerment and motivated environment by hospital management would work as an encouragement for RNs to pursue their post registration nursing degree. The findings concurred with studies by Romp *et al.* (2014) and Richards (2007), which noted that the initiation of motivational steps from the hospital administrator was important. Factors such as promoting opportunities for further study in nursing degree, promoting the staff and applying empowerment strategies contributed to the nurses' interest in pursuing their nursing degree.

Aiken *et al* (2014) research found that RNs perceived additional responsibilities as added burden to their profession once they obtained a degree. Megginson (2008) reported that nurses were of the opinion that obtaining a nursing degree was not necessary since their current qualification was adequate to pursue their nursing career (as cited in Bellfield & Gessner, 2010). However, most of the respondents from our study agreed that a nursing degree should be the basic qualification for RNs because they felt that this basic professional qualification increased their confidence and efficiency at work. This result also concurred with the findings from our literature review. Post registration nursing increased confidence and efficiency (Schwarz, 2014), improved skills of leadership and critical thinking of nurses working in a more complex work environment (Nash, 2013 & Morgenthaler, 2009). Nurses with a degree have better nursing knowledge to contribute to enhance patient's outcomes and better hospital workforce (Sarla, 2013). Increasing the number of baccalaureate prepared nurses reduces the mortality rate, increases rescue rate (Estabrooks *et al.*, 2005; Tourangeau *et al.*, 2007; Friese *et al.*, 2008 & Aiken *et al*, 2003; 2008) and according to Chang and Mark (2009) it reduces medication error incidents (as cited in Bellfield & Gessner, 2010).

As high educational cost was identified as one of the top factors deterring RNs from pursuing the nursing degree in this study, the majority of the respondents strongly agreed that the course fee for post registration nursing degree is expensive and they could not afford to pursue the post registration nursing degree with their current income. The result agreed with the finding reported by Chong *et al* (2014) and Romp (2014). Rising educational costs have driven RNs to increase their incomes by working extra shifts to ease the family economic burden in order to provide financial support to their families (Morgenthaler, 2009).

As for financial commitment, the majority of the respondents agreed that high financial and family commitment have deterred them from pursuing their nursing degree. This was supported by the studies by Lim (2012) and Sarla (2013), which noted that financial commitment for car loan or housing loan and personal or family financial commitment increased the nurses' monetary burden. The respondents from this study considered that scholarship, personal or the National Higher Education Fund will help to reduce their financial burden when pursuing their post registration degree. However, other studies by Bellfield and Gessner (2010), Lim (2012) and Nash (2013) stated that personal or government loans will increase the RNs' financial burden if taken to finance the educational fees of their studies.

More than half of our respondents agreed that they had high family expenses but they felt that this would not stop them from pursuing their post registration

nursing degree. Somehow, respondents mentioned that family support was important for them to make a move to pursue their nursing degree. A similar finding was reported by Bellfield and Gessner (2010) because they found that the RNs would advance their study if their family would support them emotionally and assist them in their educational journey. Romp *et al.* (2014) however reported that family responsibilities were the main factor that deters RNs from upgrading their educational level. Lim (2012) concurred that it was difficult for RNs to save enough money to pursue a nursing degree when they had high financial commitment for themselves and family. Further to our brief comparison analysis to the demographic data obtained with the 8 deterring factors, we found that respondents who were married were more demotivated in pursuing post registration nursing degree due to high family commitment. Those married respondents with many children had higher family commitments than those without children. These findings were similar with that of Megginson (2008) whereby family commitment and child care duties deterred RNs from furthering their higher education studies.

Regarding time constraint and high workload, many respondents agreed that their working schedules and workload prevented them from pursuing post registration nursing degree because due to the manpower shortages, RNs have to work overtime plus extra shift work if they are in a 3- shift duty, leaving them with little or no time to study and to complete their assignments (Richards, 2007; Morgenthaler, 2009 & Lim, 2012).

The majority of the respondents from this study agreed that their superior or organisation encouraged them to pursue the post registration nursing degree. They were also willing to pursue this degree if sponsorship was offered. They agreed that extra allowances and promotion opportunities were factors that could drive the RNs to pursue the post registration nursing degree. But the majority of the respondents were reluctant to take up the sponsorship as they were not willing to be tied down with a service contract. The RNs preferred to have flexible working schedules for them to pursue their study, but on contrary, they encountered difficulties to obtain leave or time off for this purpose. Therefore, this finding was consistent with Bellfield and Gressner (2010) and Chiu (2005), where they noted that hospital administrators play important roles in inspiring RNs to pursue their higher education with Nurse Managers giving more opportunities and emphasising recognition towards the nursing degree and encouraging more RNs to pursue the nursing degree. Nash (2013) also supported that many of the RNs did not pursue their post registration nursing degree due to lack of support from their work organisation.

Many respondents in this study agreed that online or distance learning post registration nursing degree will allow flexibility in study and will permit them to balance their family roles and work duties. This finding was supported by Morgenthaler (2009) and Nash (2013), where they mentioned that online or distance learning post nursing degree provided better study conditions for nurses to pursue their nursing degree. With our finding, we agreed with Halter et al. (2007), that a flexible programme delivery option especially the online programme will allow RNs the opportunity to meet their goals while balancing family and work commitment (as cited in Cathro, 2011).

Recommendations

Organisational management should consider workable measures to assist and motivate their nurses to upgrade themselves with a nursing degree. Measures include possibilities of offering scholarship, sponsorship or study loan for the RNs to overcome high educational cost and financial commitments. Incentives such as extra allowances and promotion for degree holder RNs would definitely attract more RNs to consider taking up the option to further their study. Flexible working schedules, study leave or time off and arranged overtime would also allow the RNs to have a good balance in focussing on their work and studies.

Conclusions

High educational cost, financial commitment, time constraint and high workload were the top 3 factors found to be deterring the RNs in this study from pursuing post registration nursing degree. With the recommended measures the organisation will not only benefit from securing more RNs with better professional qualification to deliver quality care to clients but will also foresee an increase in employee engagement and retention because of employees satisfaction and appreciation with an organisation who is able to provide a good future and better growth prospects for them.

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Primary hyperparathyroidism with vitamin D deficiency in third trimester of pregnancy

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Abstract: In pregnancy, the diagnosis of primary hyperparathyroidism (PHP) may be delayed due to physiological changes that occur during this period. The maternal related complications of PHP during pregnancy has been reported to be as high as 67%, whilst fetal complications up to 80% of cases.[1] The therapeutic gold standard and definitive treatment for PHP in pregnancy is minimally invasive parathyroidectomy in the second trimester. We report a case of a 22-year old primidgravida who underwent parathyroidectomy in the third trimester of her pregnancy for PHP with persistent hypercalcemia. She was also found to have Vitamin D deficiency which probably led to secondary hyperparathyroidism and made her hypercalcemia more apparent during pregnancy.

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Keywords: Primary hyperparathyroidism, hypercalcemia, pregnancy, parathyroidectomy, vitamin D deficiency

Case Report

Our patient is a 22-year old primidgravida who was referred to our hospital at 32 weeks of pregnancy for persistent hypercalcemia. She was well before her pregnancy and did not have any medical illnesses prior to that. Her initial presentation was to a district hospital during the first trimester for vomiting which was attributed to hyperemesis gravidarum. She was noted to have hypokalemia then but unfortunately her calcium levels were not assessed. At 30 weeks period of gestation, she was admitted again for premature contraction secondary to urinary tract infection. During this admission, she was noted to have parathyroid related hypercalcemia with corrected serum calcium of 3.33 mmol/L and parathyroid hormone level of 52.1 pmol/L. Despite aggressive hydration she remained hypercalcemic and was then referred to our hospital for further management.

On further assessment, she was not taking any calcium supplements or other medications that may contribute to hypercalcemia, such as lithium. She did not have any previous history of fracture or any symptoms of hypercalcemia (while on hydration). She was not aware of any family history of hypercalcemia or renal stones. Her blood pressure was 117/84 mm Hg with pulse rate of 84 beats per minute. Her voice was not hoarse and there was no palpable neck swelling or cervical lymphadenopathy. Per abdomen her uterus size corresponded to the period of gestation.

Biochemical evaluation revealed severe hypercalcemia with corrected calcium levels of 3.71 mmol/L and low phosphate of 0.61mmol/l. Her potassium level was 4.2 mmol/L while on supplements but blood gas showed metabolic acidosis with serum pH of 7.32 and HCO3 of 11.7 mmol/L which was due to nephrocalcinosis related renal tubular acidosis. The Total 25-hydroxy vitamin D level was noted to be low; 19.15 nmol/L. Her serial calcium/phosphate levels and other baseline investigations are as shown in Tables 1 and 2 respectively. Ultrasound of the neck showed hypoechoiec, enlarged parathyroid gland which was seen posterior to the left thyroid. It measured 2.3 cm x 1.3 cm. Ultrasound of kidneys showed bilateral nephrocalcinosis with no evidence of obstructive uropathy.

She was initially treated conservatively with aggressive hydration of up to 4 liters of normal saline per day with potassium supplements as well as subcutaneous calcitonin. Unfortunately her calcium levels remained elevated. In view of her persistent hypercalcemia and recent history of premature contraction, left superior and inferior parathyroidectomy as well as left hemithyroidectomy was done. Intraoperatively, enlarged left inferior parathyroid gland measuring 5x3 cm and left superior parathyroid gland measuring 6x7 mm were removed. Post operatively her calcium levels reduced gradually and was normal two weeks post surgery. Histopathology report showed nodular hyperplasia of left thyroid gland. (Figures 1 and 2). Figures 3 and 4 are sections from the left parathyroid gland which showed parathyroid adenoma.

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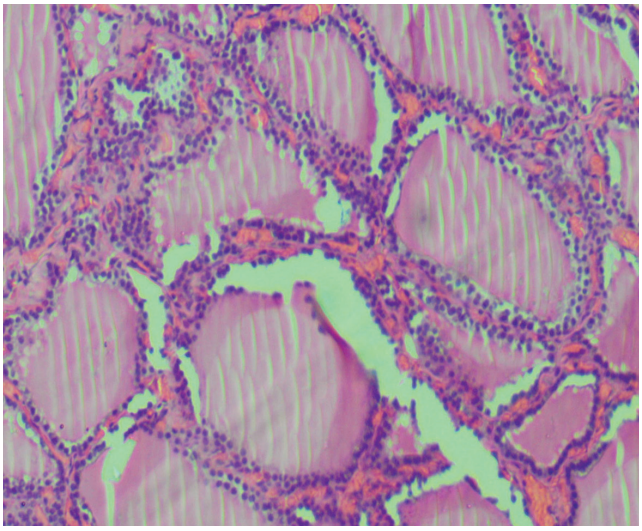

Figure 1 : (400X magnification)

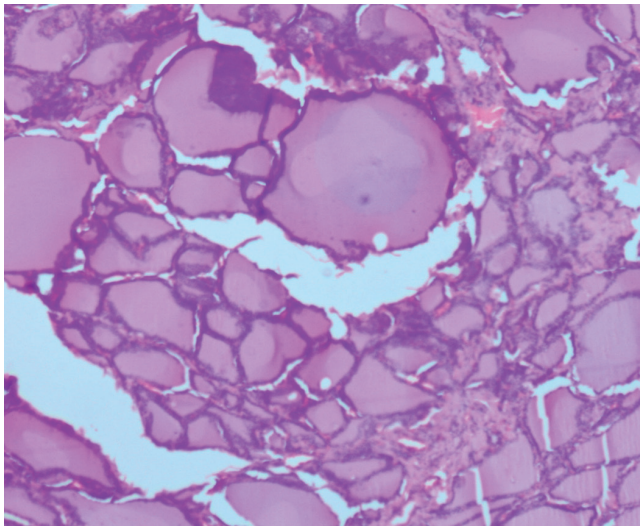

Figure 2: (400X magnification)

Figures 1 and 2: Sections from the left thyroid nodules composed of follicles of varying sizes filled with colloid. The follicles are lined by low columnar to cuboidal epithelium, few are exhibiting peripheral vacuolations. There is no evidence of malignancy seen.

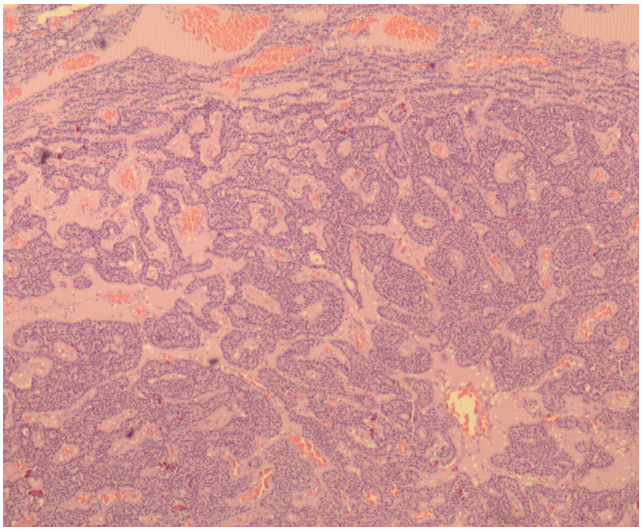

Figure 3: (100X magnification)

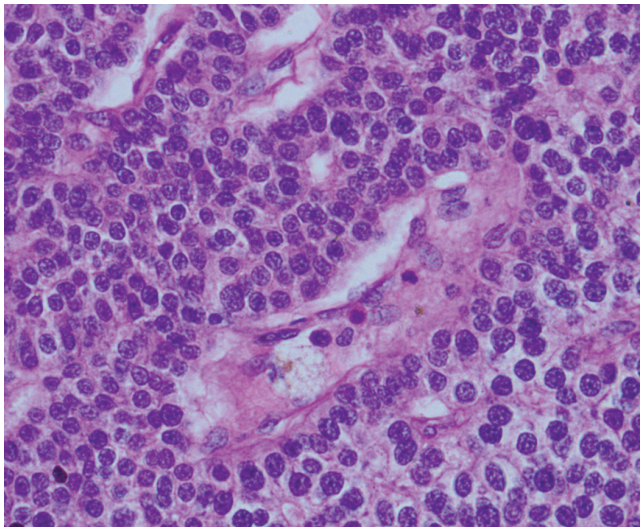

Figure 4: (400X magnification)

Figures 3 and 4: Sections showing cellular lesions. The cells are predominantly composed of chief cells arranged in solid sheets as well as micro-follicular pattern. Areas of hemorrhage with collections of hemosiderin-laden macrophages are also noted. There is no cellular atypia or evidence of malignancy seen.

The prevalence of PHP is reported to be 0.15% among general population but estimated to be as high as 1.4% if undiscovered cases are being taking into account.[2] In pregnancy, the true incidence of PHP is unknown since many cases remain asymptomatic. Some of the symptoms caused by hypercalcemia are also variable, vague and maybe wrongly be attributed to pregnancy related symptoms such as hyperemesis gravidarum. For instance in our patient, her vomiting was initially thought to be due to hyperemesis gravidarum and urinary tract infection.

Physiological changes in pregnancy in terms of calcium homeostasis may also mask the presence of hypercalcemia. These changes include intravascular fluid expansion leading to hemodilution, increase in glomerular filtration rate leading to hypercalciuria and gestational hypoalbuminemia. Maternal shunting of calcium to the fetus may contribute to a relative maternal hypocalcemia but the reduction in total maternal serum calcium levels observed during pregnancy is mainly the reflection of a decrease in serum albumin levels and consequently, a decrease in the albumin-bound fraction of calcium; the ionized calcium levels remain in the normal range during pregnancy.[3] It is therefore important to correct for lower albumin when evaluating calcium levels during pregnancies.

1,25-dihydroxyvitamin D plays a major role in maternal adaptation to provide for the fetal calcium demand. It is the main stimulus for increased intestinal calcium absorption. The level of 1,25 dihydroxyvitamin D rises during the pregnancy. Free 1,25-dihidroxyvitamin D and total serum 25-hydroxyvitamin D are also elevated. The conversion of 25-hydroxyvitamin D to its active form 1,25-dihydroxyvitamin D during pregnancy is increased by PTH-independent up-regulation of 1-alpha-hydroxylase in the maternal kidneys as well as other sources such as placenta, deciduas and fetal kidneys.[3] The paradoxical decrease in parathyroid hormone (PTH) during gestation is likely due to direct inhibition of high 1,25-dihydroxyvitamin D or by increased intestinal absorption of calcium.

Generally patients with PHP are often asymptomatic or they may have generalized non specific complaints that are consistent with their levels of calcium. The patients may not have any symptoms if their calcium levels are mildly elevated ie. less than 3 mmol/l. Those who have moderate elevation of calcium levels between 3-3.5 mmol/l may have more profound symptoms such as anorexia, nausea, vomiting and constipation. Levels that are even higher can manifest as renal impairment, mental status change and cardiac arrhythmia. Very severe hypercalcemia with calcium levels of more than 4.5 mmol/l can present with hypercalcemic crisis resulting in uremia, coma, cardiac arrest and even death.

Our patient who had PTH related hypercalcemia with concurrent Vitamin D deficiency was completely asymptomatic prior to pregnancy. Her low Vitamin D levels probably contributed to some degree of secondary hyperparathyroidism particularly when she was pregnant. This further increased her calcium levels and made her symptoms apparent (Tables 1 and 2).

Table 1: Calcium and Phosphate (PO4) results pre- and post-operatively

Parameters	Pre-op Baseline	Pre-op with Calcitonin and Hydration	Post-op Day 1	Post-op 2 weeks
Calcium (mmol/l)	3.35	3.09	2.51	1.62
Corrected calcium (mmol/l)	3.77	3.53	3.01	2.06
PO4 (mmol/l)	0.61	0.70	0.57	-
Albumin (g/dl)	19	18	15	18

Table 2: Other baseline investigations

Baseline Biochemical Parameters	Results
Urea (mmol/l)	2.0
Sodium (mmol/l)	131
Potassium (mmol/l)	4.2
Creatinine (ummol/l)	67
Magnesium (mmol/l)	0.76
Chloride (mmol/l)	108
T4 (pmol/l)	13.7
TSH (miu/l)	0.291
Total 25-hydroxyvitamin D (nmol/l)	19.15
IPTH (pmol/l)	52.1
Blood pH	7.32
Bicarbonate (mmhg)	11.7
Anion gap	15.5
Urine pH	7

During pregnancy, PHP have been reported to be associated with maternal complications up to 67% of cases and fetal complications up to 80% of cases.[2] Maternal complications include nephrolithiasis (which our patient has), radiographic bone disease, pancreatitis, hyperemesis gravidarum, muscle weakness, confusion and hypercalcemic crisis. A hypercalcemic crisis can also occur in the early post partum period due to the sudden interruption of the transplacental shunting of calcium from mother to fetus. PHP is also a disease which has been associated with endothelial damage, insulin resistance and cardiovascular disorders. Parathyroid adenoma even prior to delivery has been found to be associated with preeclampsia.[5] This is important particularly for our young patient and her future pregnancies. Fetal complications include neonatal tetany, still birth, miscarriage, premature birth, intrauterine growth retardation, low birth weight, transient hypocalcemia or even fetal demise.

Biochemical diagnostic work-up for PHP in a pregnant patient is similar to a non pregnant patient. A finding of elevated calcium level with low phosphate and detectable or elevated PTH supports the diagnosis of PTH. Evaluation of urinary calcium excretion is important to exclude familial hypocalciuric hypercalcemia (FHH) particularly in a setting of mildly elevated calcium levels with high/normal PTH and a

normal serum 25 hydroxyvitamin D level. FHH is not likely in our patient as she had moderately elevated calcium levels and already had complications of PHP i.e. nephrocalcinosis. Another interesting finding in our patient is the presence of metabolic acidosis with normal anion gap and hypokalemia. With a urine pH of 7, the most likely explanation is renal tubular acidosis. Hypercalciuria in PHP can lead to nephrocalcinosis and renal tubular dysfunction, which manifests as distal RTA.[4]

In terms of localisation studies, ultrasonography of the neck is the investigation of choice in pregnancy. The commonest cause of PHP in pregnancy is a single parathyroid adenoma, which represents 85% of all cases followed by 10% from primary parathyroid hyperplasia, 3% from multiple adenomas and 2% from parathyroid carcinoma.[1] Ultrasonography has a 69% sensitivity and 94% specificity in diagnosing a parathyroid adenoma.[2] Computerized tomography and seistamibi scintigraphy are contraindicated during pregnancy due to the possible risks of ionizing radiation to the fetus but MRI of the neck can be safely used during pregnancy.

The definitive management of PHP is surgical. In pregnancy, management of PHP depends on presence of symptoms (and severity), gestational age and patient's preference. In patients with asymptomatic mild hypercalcemia, a conservative management may be reasonable. This includes eucalcemic diet with hydration, furosemide and calcitonin. For symptomatic patients or those with calcium levels of 3mmol/l and above, immediate hospitalization with aggressive hydration and assessment of fetal well being is required. Hemodialysis is another modality of treatment for severe or refractory hypercalcemia. If all medical measures fail, parathyroidectomy is to be considered regardless of fetal gestation.

A minimally invasive parathyroidectomy during the second trimester is the therapeutic gold standard and the most definitive strategy in a patient with PHP in pregnancy. This is because during the second trimester, organogenesis is already complete and risk of preterm birth due to anaesthesia is lower. In our patient, parathyroidectomy was carried in the third trimester in view of persistent hypercalcemia above 3 mmol/l which did not improve with medical therapy.

This case underscores the importance of evaluating other causes of vomiting in pregnancy particularly if it is associated with other electrolyte abnormalities such as hypokalemia. Parathyroidectomy is a treatment of choice even in third trimester if conservative and medical therapy fail.

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Leiomyosarcoma of the breast: A case report

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Abstract: Leiomyosarcoma is a rare cancer and the presence of this type of cancer in the breast is even rarer. Due to its rarity, the management options for leiomyosarcoma of the breast are not well documented. Literature review was done to establish the best treatment options for this type of breast cancer.

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Keywords: breast cancer, leiomyosarcoma

Introduction

Leiomyosarcoma is a malignant smooth muscle tumour. It is a relatively rare form of cancer and accounts for 12% of soft tissue sarcomas.[1] They are most commonly found in the uterus, stomach, small intestine and retroperitoneum. A leiomyosarcoma of the breast is exceedingly rare. Fujita *et al.*[2] did a review in 2010 and at that time only 44 cases of genuine leiomyosarcoma of the breast have been documented in the literature. A review of literature was done to establish the best treatment management for this very rare type of breast cancer.

Case Report

The patient is a 56-year-old lady who has a sister with breast cancer diagnosed at the age of 60 years old. Otherwise there was no significant medical history. She presented with 2 months history of left breast lump which was occasionally painful. She had no constitutional symptoms. On examination there was a 6.5x5.0 cm lump in the left upper outer quadrant of the breast. Mammographic examination of the left breast revealed a large lobulated complex multi-septated mixed cystic solid mass with thickened wall. Aspiration of the lesion yielded a heavily blood-stained fluid which was sent for cytology but it only showed mainly acellular proteinacious material. A repeated cytological examination of the cystic fluid showed no evidence of malignancy. She was later counseled for wide local excision of the lump with axillary sampling. Intra-operatively the lump was vascular in nature but the cyst content was straw-coloured. Laterally the margin with the skin was very close. There were subcentimeter lymph nodes enlargements in the axilla. Histopathological examination revealed circumscribed tumour composed of spindle to oval-shaped cells arranged in short haphazard intersecting fascicles. There are numerous multinucleated giant cells. The stroma shows hyalinisation and areas of myxoid change. Mitotic figures are 18/10 high power field in cellular area. There are cleft-like spaces of ductal cells seen at the periphery. These features are in keeping with leiomyosarcoma. The lymph nodes only show reactive changes. A staging computed tomography scan revealed no evidence of distant metastases. This patient was later subjected to a left mastectomy in view of involvement of the tumour in the lateral margin. A level II axillary clearance was also done. She was also referred to the oncologist but no chemotherapy or radiotherapy was planned for her. She is being followed up closely but fortunately there was no sign of recurrence on her last follow up at 6 months.

Discussion

Sarcoma of breast accounts for only 1% of all breast cancers, and leiomyosarcoma is one of the rarest forms of sarcoma of the breast. It may present as a lump in the breast that is slow-growing and may mimic the presentation of fibroadenoma or Phyllodes tumor. It is difficult to make a diagnosis based on fine needle aspiration cytology alone. That is probably the reason our patient had two negative cytological examinations. A proper histopathological examination will confirm the diagnosis. Leiomyosarcoma is characterised by spindle-shaped cells; pleomorphic and elongated nuclei; large nucleoli; and significant mitoses. A positive staining is observed immunohistochemically with desmin, vimentin, and muscle-specific actin (SMA); whereas negative staining is seen with cytokeratin, myoglobin, and S-100[3]. The patient had positive stains for vimentin and SMA (Figures 1 and 2). The staining for desmin, however, was negative.

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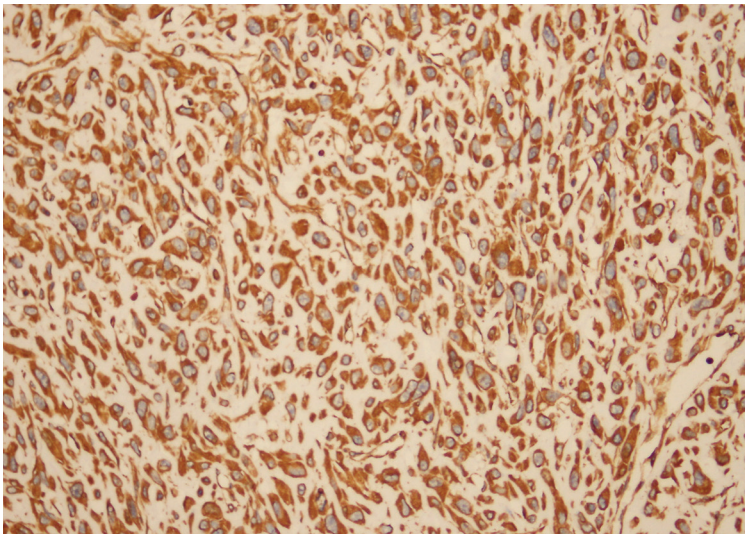

Figure 1: Histological slide of patient's breast showing positive staining with vimentin. Spindle-shaped cells and large nucleoli are also seen (400X magnification).

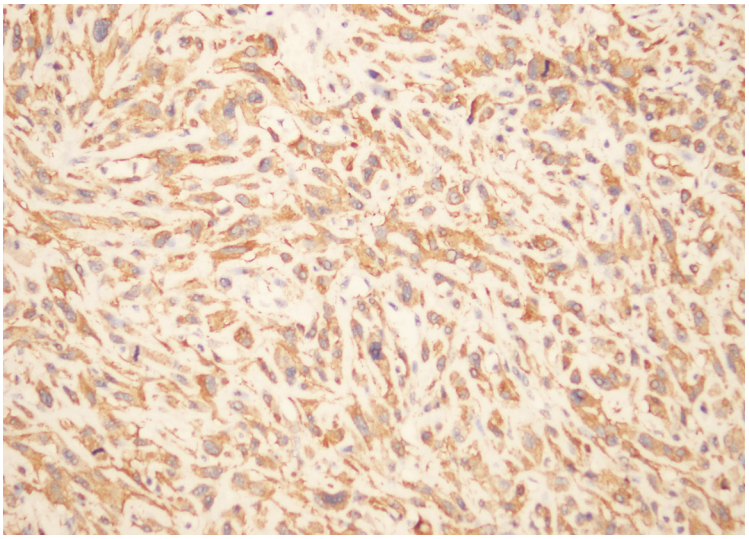

Figure 2: Histopathological slide of patient's breast tissue showing positive staining with SMA (400X magnification)

Barnes and Pietruzska in 1977[4] had suggested that several criteria are associated with poor prognosis; namely infiltrating margin, 2-3 + stromal atypia, and 8 or more mitoses per 10 high power field. The size of the tumour plays no role in prognostication factor. In our present case study, the patient has an involved surgical margin and the mitoses count was 18 per 10 high power field. Therefore she is in the high risk group and needs to be followed up closely.

There is not much difference between wide local excision and mastectomy; as long as the margin is clear, the outcome of the patient is good and risk of recurrence is reduced. Fujita *et al.*[2] recommended a 3 cm margin as an adequate margin.

As for axillary lymph node dissection, Fujita *et al.*[2] reviewed 45 case reports and no lymph nodes metastases were reported in the 15 cases where lymph node dissections were done. The patient in this study was subjected to a level II axillary lymph node dissection because initially we were unsure about the best surgical management for her. Just like previous reports, this patient also had negative lymph nodes involvement. We advocate that for leoimyosarcoma of the breast, no lymph node dissection should be done as sarcoma generally metastasizes via blood stream and rarely via lymphatic. This can save the patient from having complications of axillary surgery for example lymphoedema.

This disease is generally not very responsive to chemotherapy or radiotherapy. There is not much data which could be obtained about post operative chemotherapy or radiotherapy.

In conclusion, the mainstay of the treatment of primary breast leiomyosarcoma is still surgery. The type of surgery does not matter as long as the surgical margins are clear. Axillary node dissection is unnecessary due to no reported cases of metastases in the lymph nodes.

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