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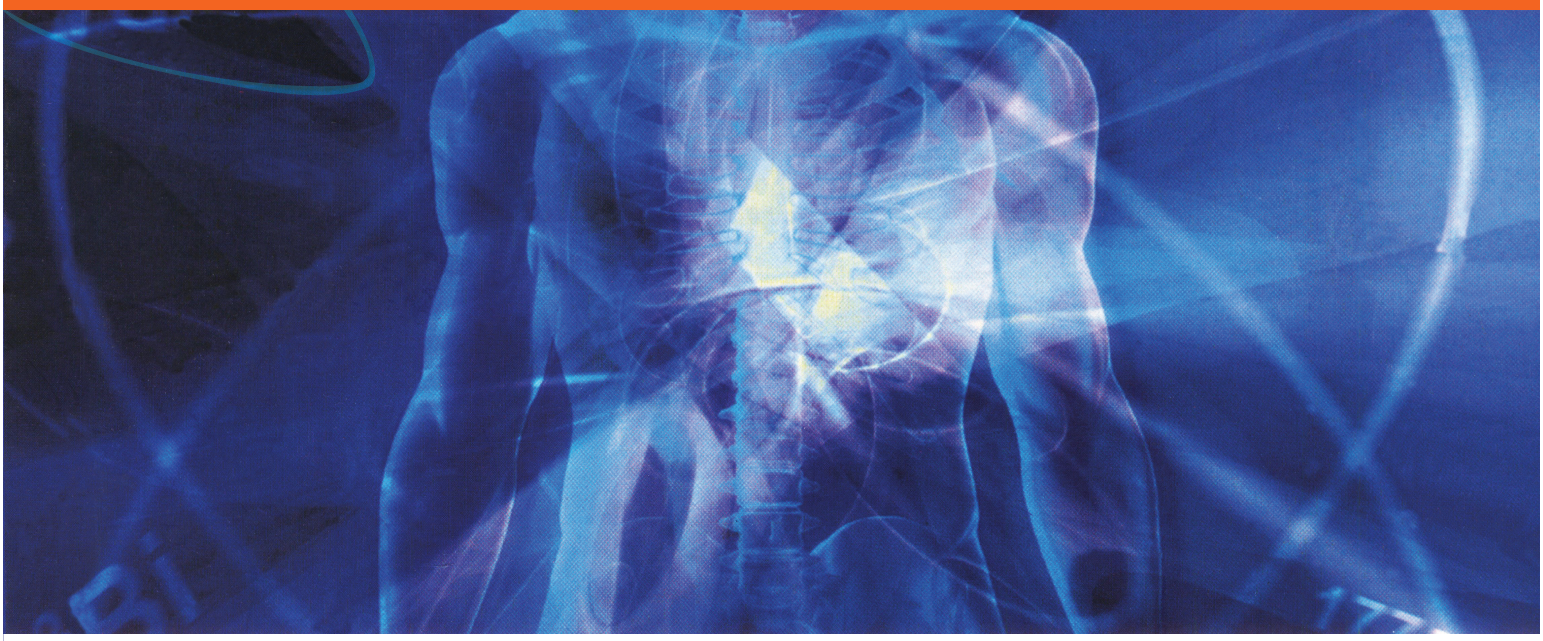

Bahria University Medical & Dental College,
Adjacent PNS SHIFA, DHA Phase II, Karachi.

Correspondence address:

Editor, JBUMDC, Bahria University Medical & Dental College, Adjacent PNS SHIFA,

DHA Phase II, Karachi, Pakistan.

Ph: +92-21-35319491-9

Website: http://jbumdc.bahria.edu.pk

JBUMDC Web Mail: editor.bumdc@bahria.edu.pk

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EDITORIAL

Importance of Electronic Learning

Ambreen Usmani

"It is through education that the daughter of a peasant can become a doctor, that the son of a mineworker can become the head of the mine, that the child of farm workers can become the president of a great nation" (Nelson Mandela, 1994).

There was a time when men travelled by horses, camels; after this carriages were made for a more comfortable ride. Decades later automobiles came into existence and slowly adapted by all. This analogy can be used in education when people wrote on stones, wood, papers and now we use computers. This is the evolution of technology, and this generation from a very young age are using technology to enhance their knowledge.[1] Now electronic learning (e-learning) has become part of the main stream in learning, teaching and assessing medical students, therefore, at its heart it is concerned with the educational uses of technology. The purpose of educational technologies is to support any aspect of medical education. Hence e-learning, e-teaching and e-assessment are interrelated but different areas of activity.[2] Common synonyms for e-learning are Web-based learning, online learning, distributed learning, computer-assisted instruction, or Internet-based learning. Integrated e-learning system in the form of virtual learning environments is becoming a norm for students of all age groups.[3] There was a time when knowledge was accessible through limited books available and through teachers, now the emergence of e-library has changed the entire scenario where the student is becoming less dependent on teachers and are more comfortable with acquiring knowledge through research. Due to this change of students' requirement teachers must also become e-teachers, some consider it as a threat to their career, others easily adopt to the ever-changing teaching strategies. Twenty years ago, the world-wide web had not been invented and computers were still some- what of a novelty. Now the 'net generation' has entered medical universities, they have grown up with these technologies and it has become integrated into their daily lives.[4] Thus, although e-learning may still seem novel and distinct to teachers, learners perceive it as far less of a shock and expect it as part of their education. e-Learning continues to proliferate, fueled by the increasingly ubiquitous availability of computers and the internet, teachers' experience in incorporating e-learning, and perhaps most importantly, learners' comfort with using education technologies. Clinician educators are increasingly using technology to complement and enhance clinical teaching and learning activities. The use of e-learning is to refer to the use of Internet technologies to deliver a broad array of approaches that enhance learners' knowledge and performance.[5]

A few examples as how novice teachers can work with online learners but this requires particular competencies and approaches of the tutor. The most important competency to be achieved by teachers is to understand and use the computer. Another way is mobile learning also known as m-learning can be used in classroom teaching by giving students tasks and ask them to find the information via internet on their cell phones.[3, 4] Mobile learning affords many new opportunities to work with learners in new contexts. Effective use of m-learning can promote many new kinds of approaches to learning. These devices include personal digital assistants (PDAs), and cellular (or mobile) phones.

A good way for novice e-teachers to begin using audio and video is to create sound or video files that can be placed on a website or VLE for download by students. These might be recordings of lectures, tutorials or clinical narratives, or they may be clinical recordings, such as heart sounds or coughs.[5]

There are many simple recording programs that can be used to create and edit sound files and convert them to the highly compressed MP3 format that allows these files to be both small and agile. For example, 'audacity' (http://audacity-ty.sourceforge.net) is a very powerful, multi-platform, and free sound-editing tool that will meet most needs. Once edited and ready for release, these files can be linked to web pages or uploaded to a VLE in much the same way that any other files (documents, presentations) are made available online. These files can then be accessed and played on a myriad of devices, including music players such as iPods, many mobile phones, PDAs, and desktop and laptop computers.[1, 3]

e-Community support- tapping into the deep-seated human will to collaborate, share and engage in community activities of many kinds. The so-called web 2.0 revolution has taken many by surprise as to how many individuals participate in content creation (Wikipedia, blogging), file sharing (YouTube, Flickr) and discussion (Facebook, instant messaging). Although participation in a medical community is an essential part of any student's entry into that community, it is debatable how such online participation is 'e-learning' per se.[4,5] We would certainly like to believe, however, that what is taught to the students is not only something to be learnt for examinations, but is also internalized, and carried over to that students' role in society. Discussion boards (also called bulletin boards or forums) are a means for participants to communicate asynchronously. This means that some one posts a message and

✉ **Dr. Ambreen Usmani**
Professor and Head
Department of Anatomy
Bahria University Medical & Dental College
Karachi
Email: ambreenusmani1@yahoo.com
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others read and post replies at some later date or time; threads of discussion thereby build up over time. Typically, the threads are track able over time, allowing users to follow many separate conversations. Discussion boards can be private (open only to a group of students), or public (open to everyone on the course).[3,5] Desktop video conferencing, more usually just called 'web conferencing', involves the connection of standard PCs or laptops with webcams, microphones etc. This format aims at bringing two or more individual users together, working through their own computers, rather than the video conferencing model of a group meeting using dedicated room-based fixed equipment.[3, 4, 5]

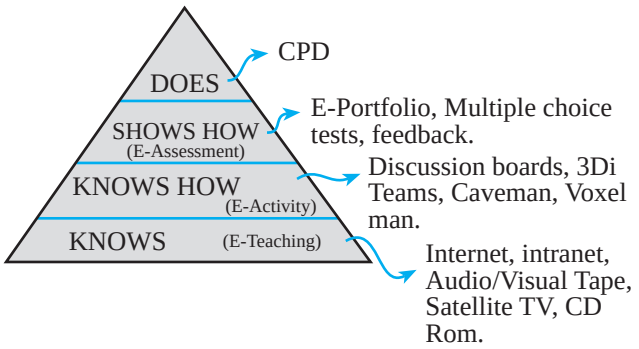
As a result, web conferencing is typically cheaper, simpler, and uses less bandwidth, but usually with lower screen resolution. Although web conferencing is now supported in many text or audio conferencing tools (such as Skype, MSN Messenger and i Chat), there is usually greater educational utility in multiple channel collaborative media tools (such as Adobe Connect, Wimba or Illuminate), which allow video, audio, chat and white boards to be used as part of a single integrated system.[3,5]

If medical universities adapt to e-learning and teaching methodologies, they should also assess them through e-assessment. This type of assessment presents particular challenges to both students and tutors. e-Assessment: the use of ICT for authoring, delivery, marking, feedback and analysis of both formative and summative student assessment. Online examination and testing (or 'quiz') tools should be applied, which usually allow for a range of question types such as MCQs, matching and ranking, single word or sentence inputs. These can be set so they can be taken only once or many times and the students' performance can be analyzed using a range of statistical tools. Most question types (except free text) can be automatically graded online. The quiz tool can often also be used for surveys and polls. Once assessments are complete, many systems have a results section or grade book, which allows staff to place marks and upload them to the VLE, and release them to students. Typically, students will see only their own marks and general statistics for the class. By this, privacy of the student may be maintained.[3,5]

Some systems may provide portfolio tools that allow students to build online repositories of their work, experiences and reflections over time as well as links to external images, documents, and media such as podcasts.[1]

To attain this system of education we must have a strong e-Logistics and e-Administration system: many e-learning applications actually support the administration and logistics of the learning environment and cognitive development. This is especially notable in medicine, where managing placements and rotations, timetabling, providing exam results, allocation to groups, tracking of content and participants, and other aspects of planning and non-educational communication with students.[2,4] Such campus environment are essential prerequisites of students' education. More widely, there are many instances where educational systems can, and should, connect to independent administrative systems and services such as registry, finance, human resources and estates and buildings. One often overlooked, but essential, administrative task that increasingly depends on the online environment, including that of audit, quality assurance and compliance, involving both internal and external scrutiny.[3,4]

Figure: 1



Source: www.google.com.pk/search?qmillertriangleofe-learning

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REVIEW ARTICLE

Vitamin D deficiency: Plethora of Etiological Factors Prevalent in Pakistan

Ayesha Saba Naz

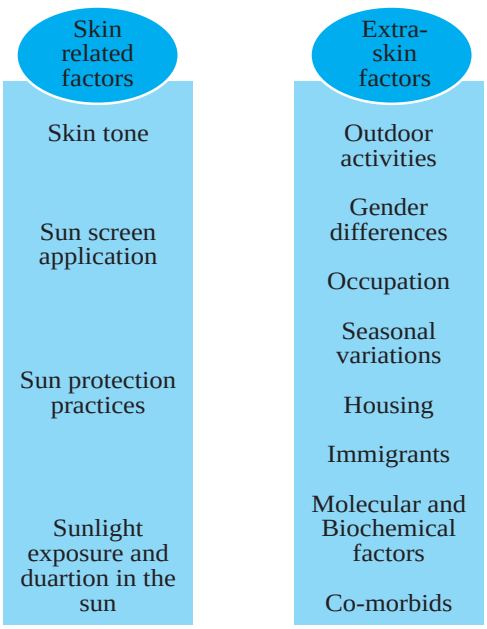
ABSTRACT:
Vitamin D, known as cholecalciferol, is a lipid soluble vitamin. Vitamin D (VD) has tremendous array of functions in the body; especially it plays a vital role in the health of the skeletal tissues. It strictly cannot be regarded as a vitamin since a substantial amount of the vitamin can be produced by the effect of sunlight on the skin. The insufficiency or deficiency of VD is growing worldwide and has assumed a pandemic situation. There are various factors contributory towards the development of vitamin D deficiency. Even in Pakistan, where sun drenched climate prevails, this alarming situation is growing and getting worse day by day. There are copious factors; like pervasiveness of sun protection practices, improper exposure to sun, lesser avenues of outdoor recreational activities, gender hindrances, biological factors etc. Lack of awareness and negligence are making this situation go even grim. In this review, the contributory factors, especially those more widespread in Pakistan are kept in view and are amalgamated in this article. Recent literature from our part of the world and after that from Asia had been preferred so that our population could connect, relate and benefit from it well.
Keywords: Vitamin D deficiency (VDD), Sunlight exposure and vitamin D deficiency, Vitamin D deficiency in Pakistan, Vitamin D deficiency in Asia, Vitamin D deficiency in women.

INTRODUCTION:

Cholecalciferol, renowned as Vitamin D; by the definition cannot be stringently considered as a vitamin, since it can be manufactured by the largest organ of the human body, the skin.[1] Cholecalciferol is a lipid-soluble vitamin. The types of Vitamin D are Vitamin- D_3 or cholecalciferol, regarded as the most active form and Vitamin D_2 or ergocalciferol. Vitamin D has tremendous array of functions to perform in the body, it escalates the absorption of calcium, helps in maintaining the serum profiles of calcium and phosphorus thus enabling the healthy metabolism and mineralization of bones.[2] It influences the bone osteoblasts and osteoclasts and aids in bone growth and remodeling.[3, 4, 5] Thus normal levels eliminate the development of osteomalacia in adults and rickets in pediatric populations. Vitamin D mediates its actions via acting upon nuclear receptors. Other documented roles are regulation of cell proliferation, differentiation and apoptosis[1], immune and neuromuscular functions.[3, 4, 6, 7] Vitamin D obtained from sunlight and the external sources; like food and supplementation is the inactive or inert form. Active form of the vitamin is acquired after successive hydroxylation. Initial hydroxylation occurs in the liver, converting it to 25-hydroxyvitamin D [25(OH)D] or calcidiol. The second one occurs in the kidneys producing the active form 1, 25 dihydroxyvitamin D or calcitriol[3]. Vitamin D is sparse in diet, and unless diet is fortified, cannot replenish the lack of vitamin D. Our diet is proficiently poor in vitamin D, as only fortification of the diet; like butter and milk can provide VD. 25-hydroxy D (25[OH]D) is the form widely used as an indicator of vitamin D level in the body. 25-hydroxy D (25[OH]D) has an advantage of long half-life, 15 days.[8] It gives a fairly good idea about the circulating levels of vitamin D but has no role in reflecting the levels of storage form. On the other hand, the active form, 1, 25 dihydroxyvitamin D or calcitriol is generally not considered to be a good indicator of vitamin D since it has a short half-life, 15 hours and the levels are tightly regulated by endocrine and mineral levels of the body. Vitamin D deficiency (VDD) is now being regarded as a global pandemic, affecting about 1 billion.[9, 10, 11] Pakistan despite of its equatorial position over the globe, has around 20-83% affected. In the review, the author is trying to sum up the factors responsible for VDD preponderant in Pakistan.

Figure-1 shows the factors affecting vitamin D levels in the body.

Figure: 1



Dr. Ayesha Saba Naz
Senior Lecturer
Department of Anatomy
Bahria University Medical & Dental College
Karachi
Email:drayeshasaba@hotmail.com
Received : 20-11-2016
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METHODOLOGY:

A comprehensive literature search was being conducted from 1990-2015. The search engines utilized were Google Scholar, Pubmed, HEC Digital Library, Springer link and Medline. The key words used were vitamin D deficiency (VDD), vitamin D deficiency in Pakistan, sunlight and vitamin D, vitamin D deficiency in Asia and vitamin D deficiency in women. In the beginning of literature search exploring with the said keywords about 50 articles were found. By adding vitamin D deficiency in Pakistan, the articles based on Pakistani data related to vitamin D deficiency (VDD) and then with the data of South East Asia were filtered. 35 original articles were found, the articles having foreign data were disregarded and so about 7 articles were filtered out and the rest were used in the write-up. In addition to the keywords that were used, the references of the articles were further elaborated to find more literature. In this piece of review, the preponderant factors of VDD were described, and the etiological reasons more common in our part of the world were explained with the help of Pakistani and Asian literature.

VDD FACTORS ASSOCIATED WITH SKIN:

Skin Tone: The complexion of skin and production of VD are closely linked .[9] Lighter skin tones are found to be associated with greater production of vitamin D (VD) due to the action of ultraviolet radiation (UVR), the vice versa is true for the dark complexioned population. Ultraviolet B (UVB) is the kind of radiation that is involved in the photosynthesis of VD. The melanin in the skin is associated to confer natural sun screen property, and thus greater protection against the penetration of UVR. It has been proven that darker skin tones (Negros) need around 6 times the standard intensity of UVR to produce VD as is produced in lighter skin tone people (Caucasians).[12] Melanin is efficient in absorbing UVB and increased pigmentation of skin containing augmented amount of melanin impedes cutaneous synthesis of VD.[13, 14, 15, 16]

Application of Sun Screen: Pakistan lies in the temperate zone of the world, and thus has a diverse climate from tropical to temperate. In most regions of Pakistan the weather tends to be relatively hot and sunny. Our country has ample sunlight, so for enhancement and maintenance of fair complexion, the use of sunscreens is widespread in our population, especially in women. Use of sunscreen is shown to be beneficial against the harmful effects of skin tan, sunburns, premature aging and the deadly danger of skin cancers. Sunscreens are enriched with para-aminobenzoic acid, which confers its beneficial effects of skin protection. Cutaneous application of sunscreens have also illustrated to reduce the photosynthesis of cutaneous VD_3 which prevents photo isomerization of 7-dehydrocholesterol to previtamin D_3 in skin.[17] Sunscreen protector of SPF 15 reduces about 99% of UVB radiation, thus greatly diminishing VD conversion.[13]

Sun Protection Practices: Sunlight is the major source of vitamin D production. UVB is associated with the cutaneous conversion of VD_3. Any factor that interferes with UVB infiltration of skin, provides hindrance in the production of VD. Sun protection practices and "no exposure to sun at all" is putting the mankind at jeopardy of developing VDD.[18] Some ethnic and religious practices, like observation of veiling are also associated with reduced sunlight exposure and thus VDD.[19, 20] But studies from Bangladesh have proved that veiling has no direct connection with the development of VDD as those who do not observe it are at equal chance of developing VDD.[21, 22, 23, 24, 25]

Sunlight Exposure and Duration in the Sun: Some people, who are better exposed to sun, use sunlight as their source of production of VD_3. UVB with a particular wavelength of 290-320 nm penetrates the skin and is linked with the production of VD. Weather, cloud cover, latitude,[19,26,27] haze, melanin content etc have association with altered productions of VD. The timing to sunlight exposure is also a key factor, the time of the day with most intense UVB radiations is 10 AM to 3 PM. Exposure during these timings have proved to produce a substantial amount of VD. 5-30 minute exposure of face, arms, legs and back with no sun protection practices twice a week is proven to produce ample amount of VD.[3,28,29] Cloud cover diminishes the intensity of UV rays to about 50% and thus its ability to produce VD .[30, 31] UVB does not pass through glass, the exposure to sunlight with glass windows does not confer any good.[3]

EXTRA-SKIN RELATED VDD FACTORS

Outdoor Activites: Healthy outcomes are produced by outdoor recreational activities, like swimming, cycling and outdoor games.[32] It has been shown that home bound subjects are prone to develop VDD.[33,34] Women and elderly are at risk of developing VDD as they have lesser chances of going outdoor.[19] On the other hand, children and younger age group are found to have higher values of VD, seemingly linked with their outdoor playing activities.[35,36,37,38]

Gender Differences: Pakistan regardless of its equatorial location over the globe and sun drenched luminous climate; VDD is prevalent and it is more common in women[21]**.** Alarming statistics show that 90% of premenopausal women have 25-hydroxyvitamin D (25[OH] D) less than 20 ng/ml. Decreased values of VD are associated with negative skeletal outcomes and predisposition of women of child bearing age towards osteopenia and osteoporosis. The literature also supports the effective role of VD in obstetrics, like prevention from premature births, neonatal neurodevelopment insufficiencies etc. Our females, as compared to their male counterparts get lesser avenues of obtaining optimal sunlight and therefore more discriminately develop VDD. Similar facts have been revealed by a study conducted in Karachi that showed VDD to be more common in women as compared to men.[39] This gender discrimination of VD levels is also shown in East African men and women, in which women are shown to have lesser values.[40,41] Studies conducted elsewhere in Asia have also established the fact of high disposition of women towards VDD.[21,22,42,43]

Occupational Behaviour: As with the people with

outdoor recreational and leisure activities, professions coupled with outdoor exposures have proved to provide better UVB exposure,[9,44,45] good exposure to sunlight and thus better values of VD. The proper, appropriately timed better contact of sunlight are allied with superior levels of 25[OH]D and consequently lesser chances of the development of VDD. Occupations like gardeners, delivery boys, daily vendors, all professions related with travelling are less susceptible to develop VDD.[9] Various studies have shown dissimilar serum values of 25[OH]D in groups of people having varying occupations, like in-house bound and outdoor working people.[9,21] The people with internal or domestic chores have shown to exhibit lower serum values of 25[OH]D as compared to those whose activities are outdoors.

Seasonal Variations: Winter season and less intensified sunlight are counterparts and they go hand in hand. In Pakistan, majority of its provinces and cities face some extreme weather like Balochistan, Islamabad, Lahore, interior Punjab and all of Khyber pakhtoon khuwa (KPK). In some parts of Pakistan smog and cloud cover diminishes the sunlight even more, like in Lahore and Sargodha. Such seasons are coupled with lower serum values of 25[OH] D as compared to the values obtained in summer,[46] as in summer there is abundance of sunlight, and photosynthesis of Vitamin D_3 ensues uninterrupted. Many studies document VD sufficiency in hot climates,[47] like a study conducted in Karachi exhibited this seasonal predilection. In winter season, the total sunshine hours get reduced. In Karachi, the total sunshine hours in January are calculated to be 271 hours, as compared to 282 hours in April and 304 hours in May.[39] The total sunshine hours in other diverse areas of Pakistan may have even more fluctuations. The photosynthesis of VD_3 and sunlight can have said to be directly proportional to each other.

Housing: Way of living and housing also plays a key role in the development of VDD. Town of residence, house architecture and avenues for the better aeration and natural light are pertinent factors in this regard. A study conducted had shown that downtown dwellers and thickly populated housing areas have positive links with the lesser amount of sunlight provision, and thus progression towards the development of VDD.[48] A study conducted in Karachi showed VD levels in posh localities like DHA and Clifton to be healthier as compared to Saddar and Gulshan-e-Iqbal, which can be accounted for the better socioeconomic background and literate attributes of the dwellers of the said areas.[49] To cater the wildly rising population, living in apartments seems to be a solution. But apartment dwellers get limited access to air and light. The same fact has been documented by another study, that showed Arabian ladies living in apartments are prone towards VDD than women living in villas.[50]

Immigrants: Substantial data is available that immigrants are at risk of developing VDD. In a study conducted in 1970 in United Kingdom (UK), 25[OH]D levels were first noted to be decreased amongst the immigrants of UK. This can in part be accounted for the total change in climate, sparse chances of obtaining sunlight,[31] and diet. Numerous researches have authenticated that migration to Western countries makes the non-western immigrants predisposed towards VDD as compared to the natives.[51,52] Oslo health study had revealed more than 90% of Pakistani immigrants to have low levels of VD as compared to 14% of their Norwegian counterparts[53]. The immigrants of origin other than Pakistan can also fit in this factual frame, as stated by the Oslo health study. The similar insufficiency can also be found in refugees, as their serum levels of 25[OH]D have validated the same results.[54] Research shows lowest levels of VDD among refugees from any region of the world to be 59% and overall more than 70% of the refugees have VDD.

Molecular Biological Factors: Although alterations in VD status are always allied with the decreased exposure to sunlight, diet, outdoor activities, but it also has positive linkages with molecular factors as well. VDD can also result due to genetic factors, notably the one genetic determinant on which research data is available is rs4588 (Styl) polymorphism, that causes faulty production of vitamin D binding protein. Literature documents the genotype of vitamin D binding protein (DBP) to affect the total 25[OH]D levels.[21] Apart from DBP, incongruity in the genes programming the vitamin D 25- hydroxylase enzyme CYP2R1 and its receptor (VDR) have also been accounted for the development of VDD.[55] rs4588 (Styl) polymorphism in the vitamin D binding protein are found to be consistent with lower levels of VD in one of the studies conducted upon the women of child bearing age in Lahore.[56,57]

Biochemical Factors: Dietetic factors play a vital role in bone homeostasis. Minerals like calcium, phosphorus and some organic factors are integral in maintenance of skeletal tissues. VD, Calcium and parathyroid hormone (PTH) are components of one cycle. Variation/ imbalance in any one can vary the levels of other components in the cycle. These three components are the key factors in normal health of the osseous/skeletal tissues. The absorption of calcium is dependent upon VD. Calcium initiates, maintains and regulates the mineralization of bones and keeps the secretion of PTH in check. The lower levels of calcium causes enhanced release of PTH, and thus PTH reverses the insufficiency of calcium in the serum by demineralization of the bone. Skeletal tissues produce Alkaline phosphatase (ALP), an isoenzyme. The raised serum levels of this isoenzyme are related with certain skeletal diseases, osteoporosis is one of them. The secretion of alkaline phosphatase (ALP) also becomes raised when PTH is trying to revive the insufficient serum calcium levels. Vitamin D deficiency has been linked with altered serum levels of several minerals. Serum Calcium is indispensable in the accrual of bony mineralization. Vitamin D insufficiency is associated with flawed mineralization of bones, secondary hyperparathyroidism and negative musculoskeletal outcomes. VDD and resulting low serum calcium level further augment this vicious cycle of secondary hyperparathyroidism.[57] Low levels of

calcium, phosphates and high levels of Alkaline phosphatase have associations with VDD but any strong positive link is yet to be established.[21] Whereas low levels of calcium and high values of alkaline phosphates (ALP) can be related to severe VDD.[31]

Comorbids: Low levels of VD are associated with comorbid, or it may be said that lower levels of VD struck affecters are at higher risk of contracting other diseases. Bone pain, osteopenia and occult osteomalacia is highly prevalent in Pakistani healthy women, mothers and in their breast fed infants.[31] VDD has also been seen in bed ridden patients, women with obstetric problems and hip fractures.[31] As in other parts of the world, Tuberculosis ranks high in increasing the global illness burden, and as an estimation responsible for 1.5 million deaths annually.[58] It had been documented in a Pakistani research that VDD may precede the onset of tuberculosis. Although it cannot be said that VDD and tuberculosis have direct association with one another. Chronic renal disease patients are at high risk of developing VDD. No association had been found between the development of hypertension and VDD.

Table: 1

Life-stage group	RDA (IU/D)	Serum 25[OH]D level corresponding to RDA
1-70 years	600	20ng/ml
70+ years	800	20ng/ml
0-12 months	400	20ng/ml

CONCLUSION:

Based upon the above described factors, lack of sunlight exposure and enhanced risk of adopting VDD, the author recommends supplementation of the vitamin as prescribed by Institute of Medicine (IOM) in table-1. These values are designed to regulate the serum value of 25[OH]D at 20ng/ml, at which maximum of the bodily needs are met by 97.5% of population[59]. VD supplementation should be advised to masses to exclude the potential deleterious effects VDD may have on our lives.

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ORIGINAL ARTICLE

Biochemical Changes In Subjects With Fatty Liver: Is There A Link?

Syed Aown Raza Shah Bokhari[1], Taimur Hussain Babar[2], Sikandar Hayat Khan[3], Mariam Hasan[4], Muhammad Junaid Khan[5]

ABSTRACT:

Objective: To evaluate the biochemical markers including serum triglycerides, ALT, and fasting plasma glucose in detection of fatty liver disease.

Methodology: This cross-sectional analysis was carried out at the department of radiology & pathology, PNS Rahat hospital, Karachi between March-2010 to February-2011.Sixty-two subjects with an ultrasonographic diagnosis of fatty liver were compared with thirty-seven subjects with normal ultrasound for fatty liver, after excluding all other abnormalities on history and examination. The comparison included measurement of biochemical abnormalities including fasting blood glucose, triglycerides, total cholesterol and alanine transaminase (ALT).

Results: The results of fasting blood glucose[{Fatty liver group=7.06 ± 3.51mmol/L}{Without fatty liver disease=5.12 ± 0.56 mmol/L} (p = 0.002)], serum triglycerides [{Fatty liver group=2.56 ± 1.33 mmol/L } {Without fatty liver disease=1.68 ± 0.97 mmol/L } (p = 0.001)] and ALT[{Fatty liver group=36.37 ± 18.12 IU/L} {Without fatty liver disease=28.15 ± 13.95 IU/L} (p = 0.026)] were significantly higher in subjects with fatty liver disease. The Receiver Operating Curve (ROC) analysis showed fasting blood glucose and serum triglycerides to have the most area under the curve (AUC) as 0.747 (95% CI: 0.647-0.847) and 0.731(95% CI: 0.622-0.840); while the other parameters have AUCs as: Serum ALT-0.650 (95% CI: 0.532-0.767) and total cholesterol-0.509 (95% CI: 0.389-0.629).

Conclusion: Hyperglycemia and hypertriglyceridemia are associated with an ultrasonographic diagnosis of fatty liver. Raised transaminase levels in subjects with fatty liver disease also suggest underlying hepatocyte damage.

Keywords: Fatty liver, Serum triglycerides, Serum ALT, Fasting plasma glucose.

INTRODUCTION:

With the emergence of obesity pandemic across the world, problems like nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH) and steatosis (fatty liver) are increasingly being encountered.[1] The presence of hepatic fat becomes not only a source of confusion during the diagnostic testing of an apparently healthy subject, but it also amounts to unnecessary stress to the patients leading to loss of technical man hours and most importantly not becoming a cost-effective option because of multiple requests for hepatitis screening and radiological investigations like repeated ultrasonography.[2]

Fatty deposition in liver has been related to excess of lipids travelling in the blood.[3,4] A lot of literature dealing with various aspect of this fat deposition states in liver has been available over the last decade.[4,5] However, the literature review will demonstrate some contrasts: Firstly, serum alanine transaminase (ALT) being a marker of hepatocyte injury has not been reported to be raised in subjects with such a diagnosis.[6,7] Secondly, there are studies which have shown variable results for differences in cholesterol and triglycerides among subjects with or without a fatty liver.[8] Thirdly, literature review does suggest that fat deposition in the liver may be due to associated insulin resistance or simply a complication of diabetes mellitus.[9] On the other side, the contrasting evidence also exists with regards to normoglycemia in a patient with underlying fat deposition in the liver.[10] Lastly, there are regional and ethnic differences which could play a differential role in associated development of fatty liver state and its associated biochemical picture.[11] A study was therefore planned to compare the results of glucose, ALT and lipid indices among subjects with and without a diagnosis of fatty liver.

✉ **Dr. Syed Aown Raza Shah Bokhari**
Consultant Radiologist
Department of Radiology
PNS Rahat Hospital
Karachi
✉ **Dr. Taimur Hussain Babar**
Consultant Radiologist
Department of Radiology
PNS SHIFA Hospital & BUMDC
Karachi
✉ **Dr. Sikandar Hayat Khan**
Chemical Pathologist
Department of Pathology
PNS Rahat Hospital
Karachi
Email: sik_cpsp@yahoo.com
✉ **Dr. Mariam Hasan**
Consultant Radiologist
Department of Radiology
KRL, Hospital
Karachi
✉ **Muhammad Junaid Khan**
Health Care Administrator
Department of Admin
PNS Rahat Hospital
Karachi
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METHODOLOGY:

This comparative cross-sectional study was carried out at the department of radiology and pathology, PNS Rahat hospital, Karachi between March-2010 to February-2011. The target population was adult subjects presented

to the department of pathology for estimation of fasting blood glucose on clinical suspicion of underlying diabetes mellitus. The inclusion list was shortlisted by excluding subjects (n=201)who were admitted, had fever or associated acute stress, acute exacerbation of some metabolic disorder, or who did not volunteer because of their commitments. A total of 304 individuals were requested to undergo further study by visiting lab in exact medical fasting status on any working day after verbal explanation of study's nature. Only 116 subjects reported for sampling till end of January-2011. On the day of lab visit, the subjects were consented about study participation, later physical examination was conducted and interviewed for the presence of history of any metabolic disorder in self and family members (parents, brothers and sisters). Afterwards these subjects were sampled for 10 ml of blood for estimation of fasting blood glucose, total cholesterol, triglycerides and ALT. After phlebotomy procedure the subjects were sent to department of radiology for ultrasonographic examination. Subjects who were detected to have an associated diagnosis on ultrasound examination were further excluded (n=19) from the study.

Ultrasongraphic Examination: Ultrasound Liver was done in supine position in fasting patients on Sonoline Ultrasound grey scale machine using 5 MHz convex probe.

Lab Analysis: Blood glucose was analyzed by hexokinase method, triglycerides by GPO-PAP method, cholesterol by CHOD-PAP method and ALT was analyzed by UV kinetic method. The instrument used in lab for analysis was Hitachi-902 (clinical chemistry analyzer).

Statistical Analysis: The data was entered into SPSS version-15. Descriptive statistics were calculated for age and gender differences. Inferential statistics required comparison of biochemical parameters including fasting blood glucose, serum total cholesterol, triglycerides and serum ALT among subjects diagnosed to have fatty liver disease or otherwise which were carried out by independent sample t-test. Binary logistic regression analysis was utilized to measure the effect of confounders like age and gender keeping fatty liver diagnosis as the dependent variable.

RESULTS:

Out of all studied cases sixty-two subjects had ultrasongraphic diagnosis of fatty liver and thirty-five subjects had normal liver on ultrasound examination. Age differences between subjects having fatty liver disease or otherwise was not significant [{Group-1: Subjects with fatty liver disease: 41.81±8.89}{Group-2: Subjects without fatty liver disease: 38.91±7.81}, (p=0.114)]. Out of 97 subjects, 42/70 males and 20/27 females had fatty liver diagnosis on ultrasongraphic examination. The frequency of finding fatty liver in hypertension, diabetes mellitus and ischemic heart disease in study subjects were 12/97, 18/97 and 9/97. The percentage of association of fatty liver disorder with metabolic diseases was 75% for hypertensive subjects (9/12), 77% in patients with underlying ischemic heart disease (7/9) and 100% with subjects with newly diagnosed diabetes mellitus. The differences between fasting blood glucose, triglycerides, total cholesterol and ALT are shown in figures 1-4. The Receiver operating curve (ROC) analysis shows fasting blood glucose and serum triglycerides to have the most area under the curve (AUC) as 0.747 (95% CI: 0.647-0.847) and 0.731(95% CI:0.622-0.840); while the other parameters have AUCs as: Serum ALT-0.650 (95% CI: 0.532-0.767) and total cholesterol-0.509 (95% CI: 0.389-0.629). Logistic regression analysis [Figure-5] did not reveal the effect of age and gender to be significant in the development of fatty liver.

Figure: 1

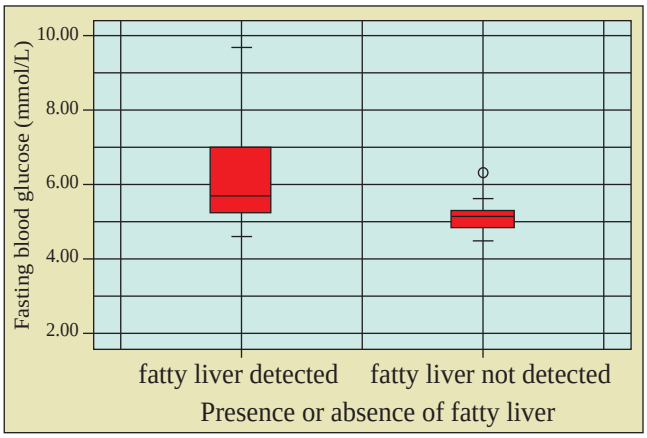

Figure-1: Differences in fasting blood glucose among subjects with fatty liver disease (7.06+3.51 mmol/L) and without fatty liver disease (5.12+0.56 mmol/L) [p=0.002].

Figure: 2

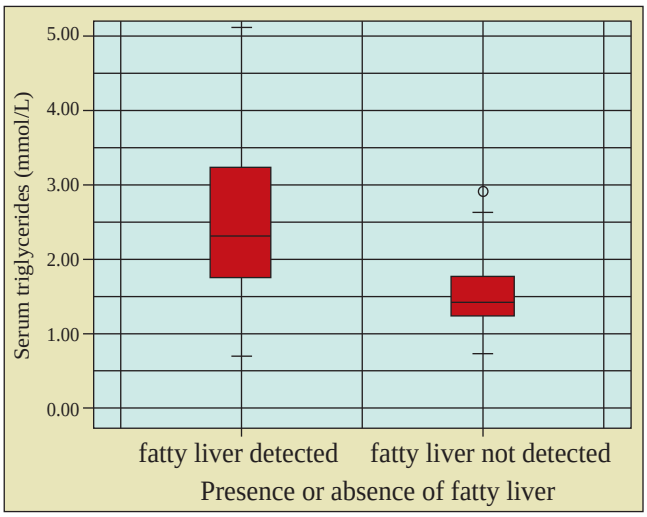

Figure-2: Differences in serum triglycerides among subjects with fatty liver diagnosis (2.56+1.33 mmol/L) and without fatty liver diagnosis (1.68+0.97 mmol/L) [p=0.001].

Figure: 3

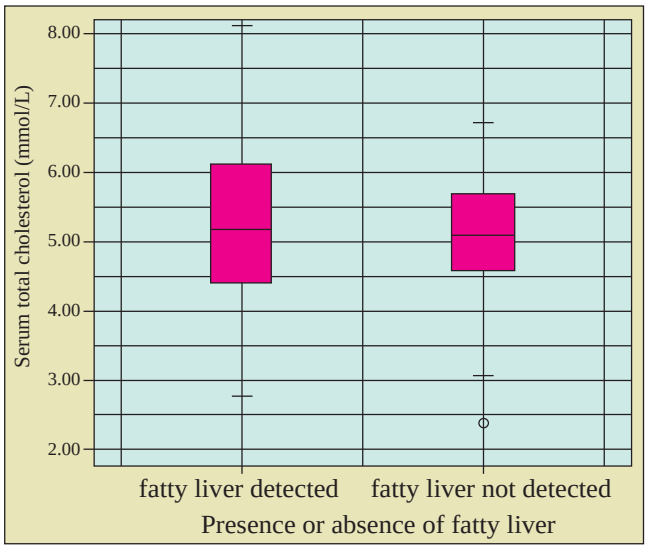

Figure-3: Differences in total cholesterol among subjects with fatty liver diagnosis (5.17+1.60 mmol/L) and without fatty liver diagnosis (4.96+0.95 mmol/L) [p=0.481].

Figure: 4

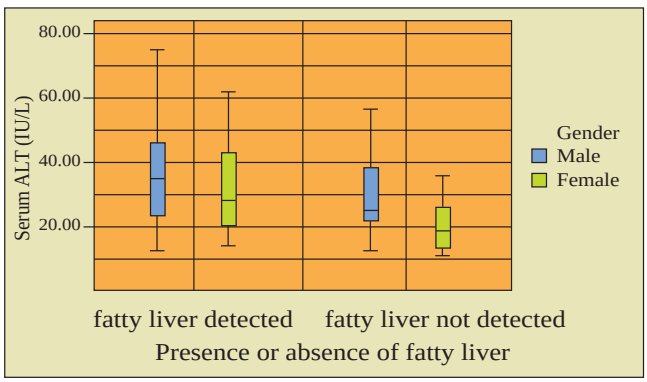

Figure-4: Differences in serum ALT among subjects with fatty liver diagnosis (36.37+18.12 IU/L) and without fatty liver diagnosis (28.15+13.95 IU/L) [p=0.026].

Figure: 5

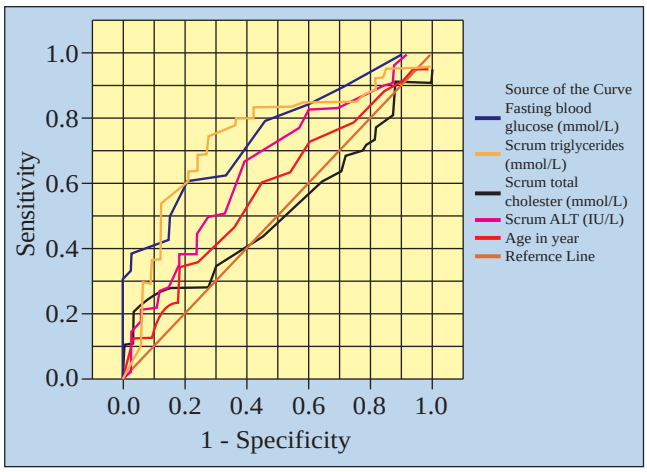

Figure-5: Receiver Operating Curve (ROC) analyais for fasting blood glucose, triglycerides, total cholesterol, ALT and age for predicting a fatty liver diagnosis.

DISCUSSION:

Our study has shown biochemical abnormalities especially hyperglycemia and hypertriglyceridemia are more frequent in subjects having an excessive fat deposition in the liver. The review of literature yields almost similar data.[3,12,13] Some studies have also demonstrated hypercholesterolemia to be associated with a diagnosis of fatty liver,[14] but we have not observed significant cholesterol differences among subjects with or without hepatic fat deposition. The explanation to this finding could be the fact that total cholesterol mainly constitutes lipoprotein bound cholesterol.These lipoprotein cholesterol in medically fasting state represent more often a depiction of hepatic lipoprotein efflux of low density lipoproteins and high density lipoproteins.[15] An insight into the fatty liver pathogenesis indicates association with higher intake of refined carbohydrates and diets rich in saturated fats.[16] These identified etiological players usually result in higher prevalence in lipoproteins containing an excess of triglycerides and may not initially disturb the other lipoprotein cholesterols in outset.[17] Upon uptake by hepatocytes, these fatty acids result in various states starting from simple ultrasongraphic evidence of extra fat in the liver to histopathological demonstration of steatohepatitis.[18] The above patterns of dyslipidemia, hyperglycemia and liver part i.e., fatty liver may be part of the wider entity of metabolic syndrome, which has a commoner metabolic basis of insulin resistance.[9] Moreover, there are studies which show observations similar to our findings in having non-significant cholesterol rise with fatty liver disease.[19] Another study by Singh et al suggests that cholesterol related differences are more encountered during the later stage of hepatic fat deposition.[20] The fact that some normoglycemic subjects also have fatty liver disease also prompts us in finding other etiological agents in the causation of this problem.[21,22] Serum alanine transaminase levels between subjects with or without fatty liver disease were not found to be significantly different. Canbakan et al have shown that hepatocytes not undergoing oxidative stress and apoptosis will probably not have an associated transaminase elevation.[23] Similarly, some other studies have demonstrated minimal transaminase differences between subjects with or with fatty deposition in the liver.[6,7,24,25] While the studies demonstrating the contrast are also available in literature.[26,27] The probable reasons to variable transaminase differences are because of evolution of disease from the stage of simple hepatic steatosis to a disease causing hepatitis and finally cirrhosis.[28] Studies have also indicated that raised serum transaminase levels may be due to associated insulin resistance in studied subjects independently of presence of hepatic steatosis.[29] Few limitations to our study must be acknowledged: Firstly, the study was a cross-sectional trial based upon non-probability convenience sampling, targeting the biochemical changes between subjects with or without fatty liver disease. Secondly, type-II error due to a small sample size can also be anticipated. It is also felt that the nature of our hospital based survey, being a cross-

sectional design should lead to a comprehensive epidemiological survey to augment or disapprove our observations.

The study may have important clinical implications: The trend of urbanization and changes in healthier life styles has led to the appearance of vast majority of asymptomatic human subjects who are diagnosed to have no other abnormality except fat deposition in the liver. Our study has demonstrated that such a random finding in apparently healthy subjects merits screening for ruling out any metabolic abnormalities like diabetes mellitus or hypertension.

CONCLUSION:

Hyperglycemia and hypertriglyceridemia are associated with an ultrasonographic diagnosis of fatty liver. Raised transaminase levels in subjects with fatty liver disease also suggest underlying hepatocytes damage.

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Metabolic characteristics of a fatty liver disease model induced by high-fat feeding in young rats. ZhonghuaGan-Zang Bing ZaZhi. 2010;18(1):54-8 doi: 10.3760/cma.j.issn.1007-3418.2010.01.013

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ORIGINAL ARTICLE

An Assessment of the Shade Differences in the Anterior Teeth According to the Age and Gender, Using Commercially Available Shade Guide

Farzana Memon[1], Diya Ram Khatri[2], Salwa Memon[3], Daud Mirza[4]

ABSTRACT:

Objective: To assess the shade differences in the anterior teeth according to the age and gender using commercially available shade guide in the local populations of Hyderabad.

Methodology: This cross sectional study comprised of 200 patients belonging to both genders ranging in age from 15 to 75 years, divided into four groups on the basis of chronological age: Group I: 15 to 30, group II: 31 to 45 , group III: 46 to 60 and group IV: 61 and onwards. Shade of the middle third of the labial surface of the anterior teeth was recorded visually using Vitapan® classical shade guide.

Data was analyzed via SPSS version 21. Descriptive statistics such as percentage, frequency distribution, cross tabulation and descriptive were included in Data analysis. The level of significance was set at <0.05.

Results: This study revealed that the most common shade recorded was A2 (45%), followed by B2 (20%) and A3 (10%). Younger patients had lighter tooth shades. Shades were darker with increasing age. The most common shade selected in age group I and group II was A2 which were represented as 52.8% and 52.9% respectively. Among males, the most common shade was A2 (47.6%), followed by B2 (19.5%) and A3 (15.9%) whereas in females most common shade was A2 (43.2%), followed by B2 (20.3%) and A1 (10.2%).

Conclusion: This study concluded that the tooth shade selection was strongly associated with both age and gender. Most common classical shade selected was A2. Shades were darker with the advancing age. Women's teeth were lighter than the men's. This information can be effective for fabrication of more life-like prosthesis.

Keywords: Aesthetics, Tooth shade, Shade guide, Prosthesis

INTRODUCTION:

In dentistry, patients are concerned not only with function but also aesthetics[1]. The word aesthetics is concerned with beauty and in dentistry aesthetics means to create a beautiful smile.[2,3] Most of the patients now demand restorations with increased aesthetics because of increasing dental awareness.[2] Aesthetics of any restoration basically needs to be considered with the parameters of surface form, translucency and shade.[3,4] Natural teeth have different shades on their surfaces.[5,6] Natural teeth shades depend on many factors, like age, gender, skin complexion and hair and eyes colour.[7] Age is the common factor. Shade selected under the type of light is also a major factor.[8, 9, 10] There are three main illuminates within any dental clinic: incandescent light, fluorescent light and day light.[11, 12] Day light has been suggested to be the most appropriate type of light for teeth shade matching.[13] Extrinsic and intrinsic staining, smoking, betel nut chewing etc, have also an effect on the teeth shade selection.[14, 15, 16]

Age of the patient has been found to have a profound effect on the teeth shade. Many studies have shown that teeth shades are darker with advancing age and vice versa.[17, 18] Darker shade means less translucent, increase in yellowness and decreased lightness with an increase in age.[19] That is the reason, during fabrication of complete denture, commonly lighter teeth shades are selected for younger people and darker for older people.[20] Another common factor is gender of the patient related with teeth shade selection. Males mostly present with darker teeth shades whereas females show lighter teeth shades.[17]

The aim of this study was to collect the demographic data regarding common teeth shades in our local population according to the age and gender. This information will be useful in fabrication of complete denture prosthesis in different age group persons as the selection of artificial teeth colour can be one of the most challenging procedures.

METHODOLOGY:

This was a cross sectional study, conducted in the Department of Prosthodontics at Isra Dental College, Hyderabad, over the period of eight months, from Jan, 2016 to Aug, 2016.

The study consisted of a sample size of 200 patients. Written consent was taken from the patients before shade evaluation. Patients of both genders were included with completely erupted permanent anterior teeth and within the age range starting from 15 years to 75 years.

✉ **Dr. Farzana Memon**
Departmaen of Prosthodontics
Isra Dental College
Hyderabad
✉ **Dr. Diya Ram Khatri**
Department of Prosthodontics
Altamash Institute of Dental Medicine
Karachi
Email: khatridk@hotmail.com
✉ **Dr. Salwa Memon**
Isra Dental College
Hyderabad
✉ **Dr. Daud Mirza**
Head, Department of Oral Pathology
Bahria University Medical & Dental College
Karachi
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They were divided into 4 groups on the basis of the chronological age: Group I: 15 to 30, Group II, 31 to 45, Group III, 46 to 60 and Group IV belonged to 61 and above.

Patients which presented with caries, any type of restoration, endodontic treatment, intrinsic or extrinsic staining, dental erosion, attrition or abrasion, fracture lines, developmental anomalies including fluorosis and orthodontic brackets or bands on the anterior teeth were excluded from study. Those female patients were also excluded who were not willing to remove lipstick and facial makeup before shade evaluation. Those patients were also excluded who had xerostomia, a history of radiation or tooth bleaching.

The shade of the middle third of the labial surface of the permanent anterior teeth was taken by using the Vitapan classical shade guide (manufactured by VITA Zahnfabrik, Bad Sackingen, Germany). Shades were taken in natural daylight preferably between 10:00 am and 12:00 noon on days with clear skies. Patients were seated on an upright sitting chair. Teeth shade readings were made at the start of an appointment to avoid the errors in shade recording due to dehydration. Shades were taken within 1 to 2 minutes and not more than 3 to 4 patients were seen by an observer in a day to overcome the effects of fatigue and tiring of the observer. Patients were draped with a grey-blue napkin and patients were asked to rinse the mouth with normal tap water before shade selection. Patients were viewed at eye-level so that the most colour sensitive part of the retina was used. Eyes were rested immediately after shade selection by focusing on the grey-blue drape for 5 seconds at a time. Teeth shades recording were made very swiftly, from an arm's length distance. Shade tabs were moistened before shade recording. Data was collected & analyzed by SPSS version 21. Descriptive statistics such as percentage, frequency distribution, cross tabulation and descriptive were included in Data analysis. The level of significance was set at <0.05%.

RESULTS:

This study comprised of 200 patients. Out of which 118 (59%) were female and 82 (41%) were male patients. They were divided into four age groups on the basis of chronology. Most of the patients fell in group I (15-30 years), which represented 44.5%, followed by group II (31-45years)35.0%, group III (46-60years) 15.5% and group IV (60+ years) 5.0% respectively. The distribution of patients according to age group and gender is shown in Table-1.

Total 16 different shades were represented in our shade guide. Out of 16, only 12 shades were recorded in this study. When considering the distribution of shade selected according to the gender, it was found that 10 shades were present in females and 10 were present in the male patients. Among males, the most common shade was A2 (47.6%), followed by B2 (19.5%) and A3 (15.9%) whereas in females most common shade was A2 (43.2%), followed by B2 (20.3%) and A1 (10.2%), as shown in Table-2.

Out of 200 patients, the most common shade recorded was A2 (45%), followed by B2 (20%) and A3 (10%) among all patients, shown in Fig-1.

While considering the distribution of shade selected according to the age groups, the results found that, the most common shade selected in group I and group II was A2, which comprised 52.8% and 52.9% respectively, whereas in group III- common shade selected was B2-35.5% and in group IV, A3-70.0% was recorded (Table-3).

DISCUSSION:

This study was undertaken to assess a relationship between the different tooth shades of the individuals according to the age and gender. Tooth shade matching can also be done using one of the two methods: one is instrumental (spectrometers, photoelectric colorimeters and colour scanners) and other is visual shade guide[21]. Both techniques have inherent inaccuracies.[15] In spite of being unreliable,[22] visual shade analysis remains the most commonly used method because it is more cost effective and quick as well.[16]

For tooth shade determination, the middle third of the tooth surface was used. The middle site of the tooth is said to be the best representative of its colour because the incisal site is most often translucent and is affected by its background while the cervical colour is modified by light scattered from the gingiva.[3, 23]

The results of this study showed that there was a significant relationship between the teeth shades and the age-groups selected. It was noted that the shades of the teeth to be darker with increasing age, which was in accordance with other studies on the subjects.[6 15, 17, 24] Hasegwa et al[18] conducted study in Japanese population, they observed decrease in lightness of the natural tooth colour at the center to the cervical site and increased yellowness with increasing age. Similar correlation was reported by Jahangirie[15] where a significant association was found between tooth colour and age of the patients, tooth tended to become darker in colour with advancing age. Esan[17] found in his study that the percentage of lighter tooth shades decreased with age and that of darker ones increased with age within an age group. Hassan[6] found that the number of patients exhibiting colours of grey and red-grey increased with advancing age. It was seen in an earlier findings by Goodkind[25] that after the age of approximately 35 years, tooth tended to become darker and more saturated in colour at center site whereas colour at cervical site remained unchanged, which may have been due to already thin enamel layer at the cervical portion of the tooth.

When considering the tooth shades in relation to the gender, our study showed that males exhibited darker shades than females of the same age group. This finding was supported by studies conducted by Esan[17]and Guo[26]. Their studies showed that gender is significantly associated with tooth shades. They found that the men were more likely to exhibit darker shades whereas females of the same age group exhibited lighter tooth shades.

A more lifelike prosthesis could be provided to the patients when certain factors like age, gender, and skin complexion, are kept in mind while selecting suitable teeth shades for the prosthesis.

CONCLUSION:

With the limitations of the current study, it can be concluded that the selection of the tooth shades is significantly influenced by age and gender. Selection of the shade is significantly related to the age of the patients, in that teeth tend to be darker in colour with increasing age. It is also significantly related to the gender, in that the males exhibit darker teeth shades than females.

Furthermore, there is a lack of published literature and limited scientific information regarding the teeth shades selection. It is suggested that further research should be carried out with different shade guides available in the market to identify any other more accurate shade guide than the one used in our study.

Figure: 1
Classical tooth shade frequency

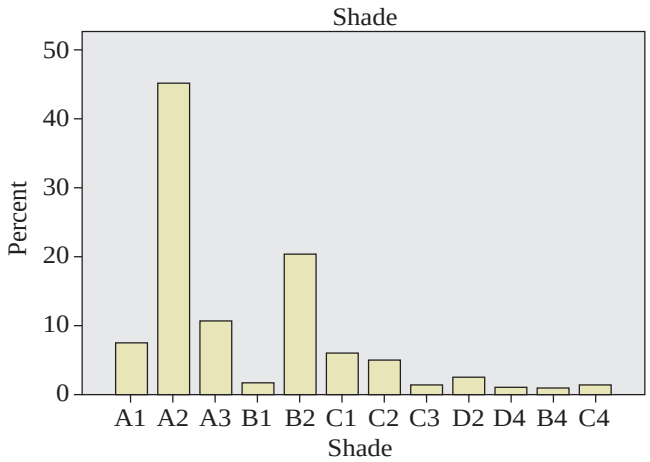

Table-1
Distribution of patients according to age group and gender

	Gender (%)					
Age Group		Male		Female		Total (%)
Group I	39	(47.6%)	50	(42.4%)	89	(44.5%)
Group II	25	(30.5%)	45	(38.1%)	70	(35.0%)
Group III	11	(13.4%)	20	(16.9%)	31	(15.5%)
Group IV	7	(8.5%)	3	(2.5%)	10	(5.0%)
Total	82	(100.0%	118	(100.0%)	200	(100.0%)

Table: 2
Distribution of patients according to shade selected and gender

Shade Selected	Gender(%) Male	Female	Total(%)
A1	3(3.7%)	12(10.2%)	15(7.5%)
A2	39(47.6%)	51(43.2%)	90(45.0%)
A3	13(15.9%)	8(6.8%)	21(10.5%)
B1	1(1.2%)	1(0.8%)	2(1.0%)
B2	16(19.5%)	24(20.3%)	40(20.0%)
C1	1(1.2%)	11(9.3%)	12(6.0%)
C2	3(3.7%)	7(5.9%)	10(5.0%)
C3	2(2.4%)	0(0.0%)	2(1.0%)
D2	3(3.7%)	1(0.8%)	4(2.0%)
D4	0(0.0%)	1(0.8%)	1(0.5%)
B4	1(1.2%)	0(0.0%)	1(0.5%)
C4	0(0.0%)	2(1.7%)	2(1.0%)
Total	82 (100.0%)	118(100.0%)	200(100.0%)

Table-3
Distribution of patients according to shade selected and age group

Shade Selected	Age Group(%)				
	Group I (15-30 years)	Group II (31-45 years)	Group III (46-60 years)	Group IV (60+ years)	Total(%)
A1	5 (5.6%)	6 (8.6%)	4 (12.9%)	0 (0.0%)	15 (7.5%)
A2	47 (52.8%)	37 (52.9%)	6 (19.4%)	0 (0.0%)	90 (45.0%)
A3	5 (5.6%)	9 (12.9%)	0 (0.0%)	7 (7.0%)	21 (10.5%)
B1	1 (1.1%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	2 (1.0%)
B2	17 (19.1%)	12 (17.1%)	11 (35.5%)	0 (0.0%)	40 (20.0%)
C1	9 (10.1%)	0 (0.0%)	1 (3.2%)	2 (20.0%)	12 (6.0%)
C2	2 (2.2%)	3 (4.3%)	5 (16.1%)	0 (0.0%)	10 (5.0%)
C3	1 (1.1%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	2 (1.0%)
D2	1 (1.1%)	0 (0.0%)	2 (6.5%)	1 (10.0%)	4 (2.0%)
D4	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)
B4	0 (0.0%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	1 (0.5%)
C4	0 (0.0%)	2 (2.9%)	0 (0.0%)	0 (0.0%)	2 (1.0%)
Total	89 (100.0%)	70 (100.0%)	31 (100.0%)	10 (100.0%)	200 (100.0%)

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ORIGINAL ARTICLE

Postmenopausal Symptoms and Perception of Quality of Life in Postmenopausal women

Habiba Sharif Ali[1], Rabel Gul[2], Bina Fawad[3]

ABSTRACT:
Objective: To evaluate the prevalence and severity of menopausal symptoms and understand the perception of quality of life and the attitudes of women towards the use of Hormone Replacement Therapy (HRT). We aimed also to establish the correlation between menopausal symptoms with age, BMI and quality of life among the postmenopausal women.
Methodology: A cross-sectional survey was conducted at the department of Obstetrics and gynecology of Ziauddin University Karachi, from June 2015 to December 2015. A total of 300 postmenopausal women between the ages of 40 and 70 years were enrolled and studied using an interview questionnaire. The questionnaire consisted of self-perception of well-being, physical activity, socio-demographic data, and information regarding HRT and modified Menopausal Rating Scale (MRS).
Results: Mean age of the subjects was 57 years, with 38 % of the study participants being illiterate. Most of the patients had mild somatic symptoms. Most frequently reported symptoms were joint and muscular pain (79.9%), anxiety and overall exhaustion (79.6%) and sweating and hot flushes (78.8%). Very few women were using HRT (12.6%). A significant link was found between women self-perception and increased weight, with severity of postmenopausal symptoms.
Conclusion: Majority of women suffer from postmenopausal symptoms but in most cases it remains untreated due to lack of awareness, hesitancy and reluctance of the treating physicians. Women self-perception of menopause affects quality of life. Those who take it positively suffer from less symptoms.
Keywords: Menopause symptoms, HRT, Attitudes

INTRODUCTION:

Menopause is a phase in women's life causing cessation of periods due to depletion of ovarian Function. It is a physiological phase which sometimes affects women's quality of life.[1] Due to lack of estrogen from ovaries, women suffer from several symptoms such as sweating or hot flushes, dryness in the vagina, disturbed sleep, depression, headache, weight gain, loss of libido, palpitations, joint and muscle pain, constipation, dysuria and urinary symptoms etc.[2]

There is increase in life expectancy of women all over the world. As a result, a large part of women's life is spent in premenopausal, menopausal and postmenopausal states and ultimately, they suffer with these symptoms. There are variations in symptoms and severity as told by postmenopausal women throughout the world in diverse studies. These variations are due to differences in attitudes towards menopause[3] and aging among different countries, ethnic groups, social groups and cultures.[4]

✉ **Dr. Habiba Sharif Ali**
Professor
Department of Obstetrics & Gynaecology
Ziauddin University
Karachi
Email: rabel5@yahoo.com
✉ **Rabel Gul**
Student Second year MBBS
Ziauddin University
Karachi
✉ **Bina Fawad**
Student Second year MBBS
Ziauddin University
Karachi
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Severity of symptoms also depends on how women take menopause that is the subjective perception. For example, African women take it most positively and complain of less symptoms compared to western women who consider menopause as a disease and illness.[5,6] Also factors such as, underlying psychological or social dysfunction can affect the experience of menopausal symptoms. Depression leads to low self-esteem and more severe menopausal symptoms.[7]

There is limited and scanty data in Pakistan on menopause or any of its associations. Few studies have been performed on the knowledge and attitude towards menopause. Our aim was to determine the menopausal symptoms and severity by means of Menopausal Rating Scale (MRS) and its association with age, weight, preceding use of hormone replacement therapy and perception of life by women.

METHODOLOGY:

A cross-sectional survey was conducted at the Obstetrics and Gynaecology department of Ziauddin University Hospital, Kemari and Clifton campuses Karachi, Pakistan, from June 2015 to December 2015. Around 300 postmenopausal women between the ages of 40 and 70 years were surveyed after taking their verbal consent using an interview questionnaire. The participants included the patients as well as their accomplices. The questionnaire contained socio-demographic data as well as information about the medical disorders such as diabetes, hypertension, cardiac and renal disease etc. from which the women were suffering. It also included women's self-perception of well-being and physical activity.

Information regarding HRT, its use in the past, Pap smear report, self-breast examination and Mammography was also included in the questionnaire. Women were also assessed on 11-item Menopausal Rating Scale (MRS), which was used to assess quality of life. The MRS is a list of 11 items (symptoms or complaints),

the severity of which can be scored on a scale of 0-4, where 0 means no complaint; 1 - mild; 2 - moderate; 3 - severe; and 4 reflects severe symptoms. It is divided into three subscales: somatic, psychological, and urogenital.

Somatic symptoms include hot flush, heart discomfort, sleeping problem, and muscle and joint pain. Psychological symptoms include depressive mood, irritability, anxiety, and physical and mental exhaustion. Urogenital symptoms include sexual problem, bladder problems, and dryness of vagina. The higher the score, the worse the quality of life.[6]

Body-mass index (BMI) was used to assess participant's nutritional status. It was calculated based on measured height and weight. BMI of less than 30 was taken as normal or over weight and BMI of more than 30 was taken as obesity.[7] Data was analyzed using Statistical Package for the Social Sciences (SPSS) software (version 20.0; SPSS, Chicago, IL, USA). Descriptive statistics were obtained to examine the general and socio demographic characteristics of the respondents. Pearson's correlation and multiple linear Regression analyses were performed to analyze the data further.

RESULTS:

A total of 300 women based on inclusion criteria were interviewed. Among these, 55 had experienced artificially induced menopause that is they had undergone total abdominal hysterectomy and bilateral salpingo-oophorctomy. The mean age of the study participants was 57.2 ± 8.4 years. These women had a mean parity of 4.9 ± 2.6 and the average duration of menopause was 10.3 ± 12. The demographic information of the target population is given in Table-1.

When asked about the use of contraceptives, 74.3 % (n=223) had never used oral contraceptives. Questions about the comorbid showed osteoporosis as the most common problem in 50% (n=150) of the respondents (Fig-1). In response to questions about physical activity, 50.3 %(n=151) were not having any regular physical activity whereas 49.7 % (n= 149) reported regular physical activity. Majority of women 81.6 % (n=245) had natural menopause and 18.4 %(n=55) had it following abdominal hysterectomy with bilateral salpingo-oophorectomy.

When asked about the recommended screening for women, 22 % (n=66) were doing breast self-examination, 11% (n= 33) got screening mammogram done and 12 % (n= 36) had Pap smear done. Questions about the use of Hormone replacement therapy (HRT) showed that only 13 % (n= 39) had used it either currently or in the past, in contrast to 87 % (n=261) of the study participants who had never used it. The main reason for non-use of HRT was that 63.3% (n= 190) had never been offered (Fig-2). The mean Menopausal rating scale score was 13.8 ± 8.2. Most frequently reported symptoms were joint and muscular pain (79.9%), anxiety and physical and mental exhaustion (79.6%) and hot flushes and sweating (78.8%). Statistically significant association (p=.05) was found on cross tabulating different variables (Table-2).

Figure: 1

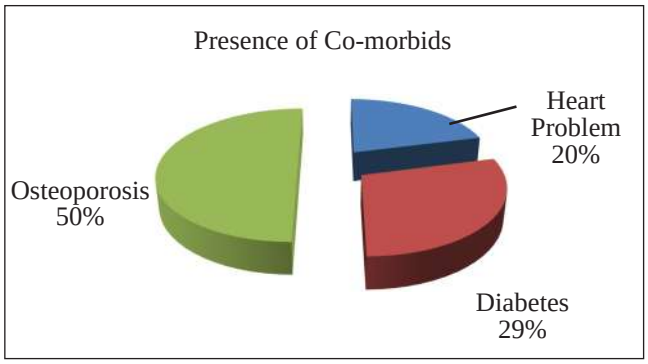

Figure: 2

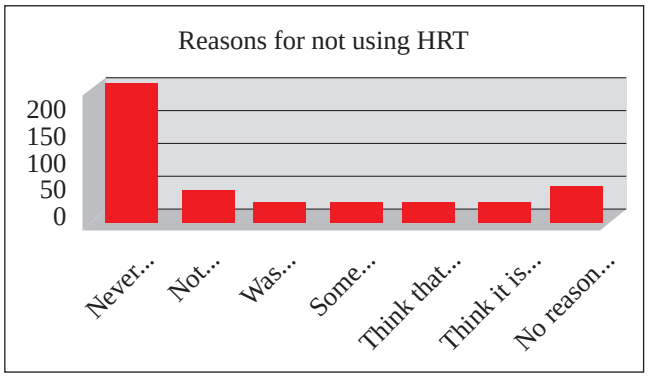

Table: 1
Demographic Information of Study Participants

Demographic factors	Category	Frequency
Employed somewhere	Yes	70
	No	230
Marital status	Single	3
	Married	227
	Widow	65
	Divorced	5
Ethnic Group	Sindhi	39
	Balochi	21
	Punjabi	96
	Pathan	62
	Gujrati	7
	Seraiki	2
	Memon	10
	Kutchi	10
	Behari	2
	Bengali	1
Educational status	No Education	115
	Primary	62
	Matric	40
	Graduation	83

Table: 2
Cross Tabulation between Level of Menopausal Symptoms and Other Variables

		Level of menopausal symptoms			
Factor	Response	Mild	Moderate	Severe	P-value
Use Of HRT(past or Current)	Yes (n=39)	73.7% (n=28)	23.7% (n=9)	2.6% (n=1)	0.362
	No (n=261)	82.9% (n=217)	16% (n=42)	1.2% (n=3)	
Age Group	36-46 yrs (n=19)	89.5% (n=17)	10.5% (n=2)	0	0.06
	47-56 yrs (n=139)	87.8% (n=122)	11.5% (n=16)	0.7% (n=1)	
	57-66 yrs (n=104)	76.9% (n=80)	20.2% (n=21)	2.9% (n=3)	
	67-76 yrs (n=27)	70.4% (n=19)	29.6% (n=8)	0	
	77-86 (n=5)	40.0% (n=2)	60% (n=3)	0	
	>86 (n=1)	100% (n=1)	0	0	
Self-perception	Very good (n=21)	100% (n=21)	0	0	0.001
	good (n=124)	91.9% (n=114)	8.1% (n=10)	0	
	Fair (n=124)	74.2% (n=92)	25% (n=31)	0.8% (n=1)	
	Poor (n=26)	61.5% (n=16)	26.9% (n=7)	11.5% (n=3)	
BMI	Less than 30 (n=174)	87.9% (n=153)	11.5% (n=20)	0.6% (n=1)	0.001
	more than 30 (n=112)	70.5% (n=79)	26.8% (n=30)	2.7% (n=112)	

DISCUSSION:

This study investigated the various menopausal symptoms and their severity among Pakistani women. The relationship of obesity, perception of life and age with severity of postmenopausal symptoms was also assessed. It also addressed the knowledge and attitude of women towards HRT. Our results revealed that the most common symptoms were muscle and joint pain, anxiety, physical and mental fatigue, hot flushes and sweating. Similar results were observed in other studies done in Asian and Saudi women.[7, 8,9,10] We found significant correlations between different variables. Worst perception of quality of life was associated with severe menopausal symptoms. Previous research had shown that the severity of menopausal symptoms was directly related to the approach of the women towards menopause. Women who thought negatively about menopause experienced more severe symptoms compared to women who had thought positively of it.[11] The prevalence of Obesity is increasing throughout the world and the problems worsen in women between the ages of 55 and 64. Hypoestrogenism is an important reason for obesity in postmenopausal women.[12] Compared with other studies showing increasing prevalence of obesity among menopausa women,[12, 13] we found that 60% of our women had a BMI of less than 30 while 40% had a BMI more than 30. It is known that chances of severe postmenopausal symptoms are more with obesity[11]. A Saudi study also found a strong correlation between obesity and severity of menopausal symptoms.[7]

We found a positive correlation between obesity and severity of menopausal symptoms. Despite fear of cancer of breast, only 22 percent performed self-breast examination and 11% had at least one mammogram. Whereas a study done in an Asian population reported 70% of the women performed self-breast examinations and 47% of women underwent mammogram.[13] Hormone replacement therapy (HRT) is being used by women for a while and is considered effective for symptoms of menopause especially for osteoporosis, cardiovascular diseases and for prevention of Alzheimer's disease.[15] However, the results of large trials, namely, the heart estrogen progestin replacement study (HERS),[16] and the women health initiative (WHI),[17] found no advantages of HRT in prevention of heart disease. The results of WHI trial has created a lot of controversies regarding the use of HRT resulting in the loss of confidence among the physicians and patients. However, studies especially from Europe indicate a rise in the use of HRT in the previous ten years,[18,19] probably because of better education status, clear guidelines on the use of HRT and

socioeconomic and health status of their population.[19] Most of the women in our study had never used HRT. Lack of knowledge about HRT was the most important reason for its unpopularity. This was similar to the findings in other studies.[2, 21,22] The lack of awareness of HRT might be due to the negative attitude of the physicians towards HRT. We used The Menopause Rating Scale (MRS) which is a health-related Quality of Life (HRQOL) scale developed in the early 1990s. It is considered to be a standardized HRQOL scale with good psychometric characteristics.[6]

CONCLUSION:

Majority of the women in our study experienced postmenopausal symptoms but did not treat them, as they believed menopause to be a natural process, or lacked awareness due to illiteracy and poverty. The association between obesity and severe postmenopausal symptoms requires increased attention and a multidisciplinary approach to women's health to prevent increased morbidity and mortality in these women. Public health efforts should focus to address the controversies regarding the use of HRT and efforts should be made to change the approach of health care providers to HRT. The aim should be to increase awareness on HRT and promote its use among physicians and the general population and public access to HRT should be ensured.

DISCLOSURE:

There is no conflict of interest in this work.

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ORIGINAL ARTICLE

Titrated Oral Misoprostol Solution Versus Intravenous Oxytocin for Augmentation of Labour

Umbreen Idrees[1], Sara Ali[2], Ayaz Ahmed[3], Sajjad Sabir[4], Ammarah Saeed[5]

ABSTRACT:

Objective: To compare the efficacy of titrated oral mis oprostol solution with intravenous oxytocin for augmentation of labour in term primigravidae in active phase of labour with inadequate uterine contractions.

Methodology: This randomized control trial was conducted in the department of Gynaecology and Obstetrics, Pakistan Institute of Medical Sciences, Islamabad, over a period of six months from 14-April to 13-October, 2014. A total of 760 (two groups of 380 each) primigravidae, between age 20-39 years, who had completed 37-42 gestational weeks by dates, or by ultrasound scan, with regular contractions and an effaced cervix dilated between 3-4 cm, and who later developed inadequate uterine contractions during the first stage of labour were included in the study. Group A received titrated oral misoprostol solution 200µg tablet dissolved in 200ml tap water and 20ml (20µg/hour) and group-B was given Intravenous oxytocin (10 units in 1000cc Hartman's solution at 8 drops/minute, doubling every 30 minutes up to a maximum of 64 drops/min for 2 hours).

Results: Mean (±SD) age of the patients was 26.4±4.4 and 26.6±4.6 years in group-A and B respectively. In group-A, 322 patients (84.7%) and in group-B 326 patients (85.8%) were delivered vaginally. Mean (±SD) augmentation to delivery interval was 293.82±99.36 and 311.65±106.73 minutes in group-A and B respectively. Mean (±SD) gestational age in group-A was 38.82±1.32 and in group-B 38.83±1.09 week. Caesarean section was performed in rest of the patients in both groups. There was no significant association between mode of delivery in both groups (P-value= 0.682).

Conclusion: Labour augmentation with titrated oral misoprostol or intravenous oxytocin resulted in about similar rates of vaginal delivery.

Keywords: Augmentation of labour, Titrated oral Misoprostol, Intravenous oxytocin.

INTRODUCTION:

The problems of prolonged labour, both for mother and foetus have been perceived for long time. The mother is presented to high risk of infections, ketosis and labour dystocia while embryo confronts the threat of infections, asphyxia and unnecessary cranial embellishment. The idea of dynamic management of labour has affected the obstetricians to change their standpoint with respect to the administration of first phase of labour.[1] Significant relationship has been stated between active management of labour, low occurrence of prolonged labour and low caesarean section rates.[2] Although, strategies for increasing uterine contractility, for instance amniotomy and oxytocin have been shown to accelerate cervical dilatation, yet these methods are not without complications.[3]

Spasmolytic and spasmoanaelgesic mixtures are administered to facilitate dilatation of cervix and to shorten the first stage of labour.[4-8] A perfect antispasmodic for increasing speed of cervical dilatation ought to have a brief and enduring activity, no adverse effects on uterine contractility and be free from uterine inertia with minimal adverse effects on mother and foetus.[9] Phloroglucinol is one of spasmolytic, principally used for gastrointestinal colic.[10] The medication was widely used during 1970s and early 1980s for augmentation of labour.[4] Other spasmolytics, such as misoprostol are also being used, which is easy to administer, with fewer side effects, such as nausea, vomiting, diarrhea and fever.[3,4]

The use of spasmolytic is increasing day by day in all clinics and hospitals indiscriminately, and there is no definite study to show the exact dose required, when to be given, and its effects on the mode of delivery. Hence this study was conducted to evaluate the effect of misoprostol in labour so that its use can be promoted further and guidelines can be provided for the safe use of drug.

METHODOLOGY:

This was a randomized control trial conducted in the Department of Gynaecology and Obstetrics, Unit II, Maternal and Child Health Centre, Pakistan Institute of Medical Sciences, Islamabad. Study was done over a period of six months from 14-April-2014 to 13-October-2014.

A total of 760 (380 in each group) pregnant women of age 20 to 39 years, who had completed 37-42

✉ **Dr. Umbreen Idrees**
PAF Hospital Samungali
Quetta
Email: umbreenemmad@hotmail.com
✉ **Dr. Sara Ali**
Railway hospital
RWP
✉ **Dr. Ayaz Ahmed**
PAF Hospital Samungali
Quetta
✉ **Dr. Sajjad Sabir**
PAF Hospital Samungali
Quetta
✉ **Dr. Ammarah Saeed**
PAF Hospital Samungali
Quetta
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gestation weeks by dates or by ultrasound scan,with regular contractions (3 in 10 min); primigravidae with an effaced cervix, dilated between 3-4 cm, and who later developed inadequate uterine contractions (two or less compressions every 10 minutes) in the course of the first stage of labour were enrolled in the study. Adequate uterine contractions were defined as occurring every 2-3 minutes and lasting 60-90 seconds. All the pregnant women with previous history of any uterine surgery, for example, myomectomy, previous history of allergy to misoprostol and any contraindication of augmentation of labour such as foetal distress, cephalopelvic disproportion (CPD) and mal-presentation were excluded from the study. Data was collected on a pre-designed proforma by fourth year post graduate. Written consent was taken from eligible women. Consent was taken from the hospital ethical committee. All the eligible patients were randomly assigned into two groups by lottery method. Group A received titrated oral misoprostol solution (200µg tablet dissolved in 200ml tap water and 20ml (20µg/hour) until passable uterine contraction was accomplished). If contraction did not occur even after four hours (4 doses), the dose was boosted to 40µg and was repeated every hour until uterine contractions occurred. Once uterine activity was adequate over 1 hour, no further misoprostol was administered. If contractions subsequently became inadequate, hourly doses of misoprostol solution were started at 10µg/hour, which were increased to 20µg/hour as much as 40µg/hour based on uterine responsiveness. The maximum dose of misoprostol was 1600µg. Group B was given intravenous oxytocin (10 units in 1000cc Hartman's solution at 8 drops/minute doubling every 30 minutes up to a maximum of 64 drops/min for 2 hours).

Once labour augmentation had begun, partogram was maintained to observe the progress of labour and to keep a record of the maternal vital signs, foetal heart rate, color of liquor (if meconium stained) and the dose of the uterotonic administered. All data was entered and analyzed using SPSS version 18. Mean ± SD was computed for all the quantitative variables. Chi Square test was applied to assess significant association of maternal age and mode of delivery in the two groups. P-value<0.05 was considered statistically significant.

RESULTS:

Mean age of the patients was 26.4±4.4 and 26.6±4.6 years in group A and B respectively. Mean augmentation to delivery interval was 293.82±99.36 and 311.65± 106.73 minutes in group A and B respectively. Mean gestational age in group A was 38.82± 1.32 and in group B was 38.83± 1.09 weeks (Table-1). Majority of the patients in both groups were between 20-30 years of age. In group A, 322 (84.7%) patients and in group B 326 (85.8%) patients delivered vaginally. Caesarean section was performed in rest of the patients of both group, however there was no noteworthy association of maternal age and mode of delivery (P-value=0.579 and 0.682 respectively, Table-2).

Table: 1
Characteristics of study participants

Variables	Group A Mean ±SD	Group B Mean± SD
Maternal age (years)	26.4± 4.4	26.6 ± 4.6
Augmentation to delivery interval (min)	293.82± (99.36)	311.65 ± (106.73)
Gestational age (weeks)	38.82± 1.32	38.83± 1.09

Table: 2
Distribution of maternal age and mode of delivery between both the groups

	Group-A Titrated oral Misoprostol		Group-B Intravenous Oxytocin		P-value
	n	%	n	%	
Maternal age (years)					
20-30	311	81.8	305	80.3	0.579
31-39	69	18.2	75	19.7	
Mode of delivery					
Vaginal delivery	322	84.7	326	85.8	0.682
Caesarean section	58	15.3	54	14.2	

DISCUSSION:

In extended labour, high infection hazards, ketosis and labour dystocia are the problems faced by mothers whereas; foetus confronts the hazard of infection, asphyxia and un-due cranial molding.[1] It has been reported that in numerous developed countries, caesarean section birth rates are above 20%.[11] Data was collected from 150 countries over 24 years (1990-2014) and reported overall birth rate by C-section to be 15%, fluctuating from 6% in the least developed region to 27.2% in the utmost established county.[12] The elementary finding adding to the high rate of caesarean section in nulliparous ladies is dystocia or delayed labour. An approach of early amniotomy with administration of oxytocin to evade postponement in labour advancement is related to an inconspicuous diminishment in the rate of caesarean sections.[13] No significant difference has been reported in caesarean delivery rate, neonatal outcome, and maternal outcome between the low and high doses of oxytocin on labour extension with the exception of amplification of labour interval.[14] However, intravenous infusion of oxytocin should be controlled through an intravenous pump machine and it might be too demanding in specific settings. Various trials have revealed that misoprostol is a successful operator for cervical maturing and labour advancement. A study done to assess the effect of orally administered misoprostol versus titrated intravenous oxytocin for labour initiation in females

with good cervical condition (Bishop Score of =6) demonstrated no benefit with higher likelihood of uterine hyper stimulation.[15]

Therefore, orally administered misoprostol of fixed dosage without individualization is not an ideal choice. In patients with unfavorable cervical status, the idea that titrated oral misoprostol administration is related to lower frequencies of uterine hyper stimulation and caesarean births than vaginal misoprostol for labor impelling is settled.[16]

Since titrated oral misoprostol solution is less demanding to administer than titrated intravenous oxytocin, we deliberated that it was worth directing this randomized controlled trial to look at the ideal treatment regimen for labour augmentation. Vaginal delivery within 12 or 24 hours is the most vital clinical factor. We found that there was no statistically significant difference in percentages of vaginal deliveries between both the groups. Therefore, titrated oral misoprostol solution can be considered as an effective alternative method for labour augmentation.

In another study, complete vaginal delivery occurred within 12 hours for 92 (78.0%) and 97 (85.8%) women in the misoprostol and oxytocin group respectively (P=0.121). However, for vaginal deliveries within 24 hours, no significant differences were observed between the two groups.[2] Sadaf et al reported no significant difference in side effects and neonatal outcome between both the groups, therefore concluded that oral misoprostol might be used as an alternative for escalation of labour.[17]

Another study reported higher failure of induction, lesser induction to delivery duration in oxytocin group than misoprostol group, whereas maternal and foetal complications were similar in both the groups.[18] Less failure to induction in misoprostol group was observed as compared to oxytocin group, with comparable maternal and foetal complications in both groups, but shorter induction-to-delivery time was reported in misoprostol group than oxytocin group.[19]

Several studies reported shorter admission to drug interval in misoprostol group, approximately equal time between induction of augmentation and delivery; and alike maternal and neonatal outcomes in both misoprostol and oxytocin groups.[20,21] Another study reported shorter induction-to-delivery time in misoprostol group but equal proportions of neonatal outcomes, as well as vaginal and caesarean delivery in both misoprostol and oxytocin group.[22] In contrast to our study, another study has demonstrated lower caesarean rate and, induction to delivery period in misoprostol group.[23,24] The findings of our study were similar to Shaheen et al, who reported nearly comparable complications and same ratio of vaginal and caesarean delivery in both the groups. The most common reason of caesarean delivery was dystocia in oxytocin group and foetal distress in misoprostol group (P-value<0.01).[25]

CONCLUSION:

Winding up the topic, labour augmentation with titrated oral misoprostol and intravenous oxytocin resulted in about analogous rates of vaginal delivery. In addition, misoprostol leads over oxytocin in different aspects like longer shelf life, stability at room temperature, and in ease of administration.

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ORIGINAL ARTICLE

Protective Effect of L-Arginine on Streptozotocin-Induced Diabetic Nephropathy in Albino Rat

Yasmeen Mahar[1], Humera Waqar[2], Sahal Salman[3]

ABSTRACT:

Objective: This study was designed to evaluate the protective role of L-arginine on body weight, and absolute and relative kidney weight of Streptozotocin (STZ)-treated albino rats.

Methodology: This experimental study was conducted in the department of Anatomy, Basic Medical Sciences Institute (BMSI), Jinnah Postgraduate Medical Centre (JPMC), Karachi, from February to March, 2010. In this study, 30 male albino rats were divided into 3 groups, containing 10 animals each. Group-A was treated as control. Group-B animals received STZ in a dose of 37 mg/kg intraperitoneally (I/P) only once at the start of experiment. Group-C received L-arginine orally in a dose of 0.3 mg/100 gram (G)body weight/day a week before STZ treatment. Body weight of animals was calculated at start and end of the study period, along with absolute and relative kidney weight and serum glucose level.

Results: There was a highly significant increase in serum glucose level in group B animals when compared to the control group A. In group C, the serum glucose levels returned near to control. The final body weight of group B animals decreased significantly when compared to their initial weight, as well as when compared to control. The data also showed that there was a significant decrease in absolute kidney weight whereas, significant increase in relative kidney weight in group B animals when compared to group A animals respectively. There was significant restoration of body weight, and absolute and relative kidney weight in group C animals receiving L-arginine along with STZ.

Conclusion: Our findings conclude that L-arginine as a nitric oxide donor and as an antioxidant, plays a significant role in preserving renal morphology in streptozotocin-treated hyperglycemic rats.

Keywords: Streptozotocin, Kidney, L-arginine, Hyperglycemia.

INTRODUCTION:

Diabetes mellitus is a metabolic syndrome with chronic hyperglycemia due to insulin deficiency.[1] Diabetic nephropathy is an important cause of end-stage renal failure. The pathogenesis of diabetic nephropathy involves vasodilatation in the pre- and post-glomerular arterioles and then, final irreversible vasoconstriction of the glomerular arterioles, which results in reduced blood flow and glomerular filtration rate.[2] Hyperglycemia is nephrotoxic. Diabetes mellitus affects more than 120 million people worldwide, and it is estimated that it will affect nearly 400 to 500 million people by year 2030.[2,3] STZ results in hyperglycemia in rats within 72 hrs.[4] It is a pancreatic ß-cell toxin which induces rapid and irreversible necrosis of these cells. The mechanism of STZ-induced ß-cell injury involves excessive reactive oxygen species (ROS) production, lipid peroxidation, protein oxidation and DNA damage leading to ß-cell death.[5] Formation of ROS is thought to be a mediator of cytotoxic actions of STZ leading to oxidative stress, which may be one of the stresses influencing the morphology of kidney.[6] Most previous studies have shown that in rodents, STZ-induced hyperglycemia results in a reduced response to insulin, despite increased numbers of insulin receptors.[7] Studies in animal models of STZ-induced hyperglycemia indicate that antioxidants improve insulin sensitivity[8]. L-arginine is the substrate for the synthesis of nitric oxide (NO), and it has direct anti-oxidant activity.[9] It is an essential amino-acid which participates in many important biochemical reactions associated with normal physiology of the organism. Exogenous L-arginine increases NO production in a variety of cells. It is both a NO precursor and donor.[10] Previous studies have demonstrated that endogenously generated NO is involved in the modulation of corticosterone production and that adrenal NO synthase activity is dependent on extracellular L-arginine.[11] The purpose of this study was to evaluate the protective role of L-arginine on the morphological changes on the kidney along with improvement of insulin resistance in STZ-induced albino rats.

✉ **Dr. Yasmeen Mahar**
Assistant Professor
Department of Anatomy
Bahria University Medical and Dental College
Karachi
Email: dryasmeenmahar1@hotmail.com

✉ **Dr. Humera Waqar**
Senior Lecturer
Department of Anatomy
Bahria University Medical and Dental College
Karachi

✉ **Sahal Salman**
Medical student
Ziauddin University
Karachi

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METHODOLOGY:

This study was conducted in the department of Anatomy, BMSI, JPMC, Karachi, for a period of 6 weeks, after obtaining ethical approval from Feb 2010 to March 2010. In this study, 30 young, healthy male albino rats, weighing around 250-300 G, were obtained from the animal house of BMSI and divided into 3 groups, each containing 10 animals. All the animals were kept under observation for one week prior to the beginning of the study for the evaluation of their health status. Food and water were supplied ad libitum. Group-A was taken as control. Groups-B and C animals were fasted overnight and administered STZ intraperitoneally in a dose of 37

mg/kg body weight.[12] dissolved in freshly prepared 1ml of Citrate buffer at 4 pH only on the first day of the experiment. Group-C received L-arginine orally in a dose of 0.3mg/100 G body weight/day[13] dissolved in 5cc of distilled water, one week before administering STZ. The serum glucose of the rats was measured at the start of the experiment and then twice weekly by glucose oxidase method from the tail vein by using a glucometer.[14] The animals were weighed and sacrificed at the end of the treatment period by using ether anaesthesia. Abdomen was opened by midline incision and both the kidneys were exposed and carefully dissected out. The absolute weight of the kidneys was recorded on Sartorius balance. The relative weight of kidney was calculated with the help of formula.[15] The results were evaluated by student "t" test. P-value was considered for significant differences.

RESULTS:

The mean values of serum glucose level in control group A at the start and the end of the treatment were 118.3±4.1 and 121.3±4.1 mg/dl respectively. In STZ-treated group B animals, the values of serum glucose level were 117.3±4.2 and 702.0±48.21 mg/dl respectively. The data showed that there was highly significant increase ($P<0.001$) in serum glucose in group B when compared to the corresponding control group A. In L-arginine with STZ-treated group C, the serum glucose levels were 115.1±3.3 and 195.3±7.4mg/dl respectively, which showed highly significant decrease in final blood sugar when compared with final blood sugar level of group B animals (Table-1). The animals of group A showed insignificant change in weight at the end of experimental study. The mean values of body weight in STZ-treated groups B were 276.4 and130.3 G respectively. The data showed a significant decrease in body weight ($P<0.001$) when group B final body weight was compared to its initial body weight as well as group A final body weight (Table-2). In STZ and L-arginine treated group C, the mean body weight at the end of study was 202.6G, which showed significant increase as compared to final body weight of STZ-treated group B animals (Table-2). The mean absolute and relative weight of kidney in control group A animals were 0.563mg and 0.249 mg respectively, while absolute and relative kidney weight in group B were 0.491 mg and 0.378 mg respectively (Table-3). There was insignificant decrease in absolute kidney weight in group B animals, whereas a significant increase in relative kidney weight in diabetic rats of group-B when compared with corresponding control group-A. The mean absolute and relative kidney weight in group C animals were 0.513 mg and 0.216 mg respectively (Table-3) which showed significant decrease in relative kidney weight when compared to STZ-treated group B animals depicting protective effect of L-arginine.

Table-1
Mean Serum Glucose (mg/dl) In Different Groups of Albino Rats

Groups	Initial Serum glucose (mg/dl)	Final Serum glucose (mg/dl)
A (control)	118.3±4.1	121.3±4.1
B (STZ-treated)	117.3±4.2	702.0±48.21
C (STZ+L-arginine)	115.1±3.3	195.3±7.4

Table-2

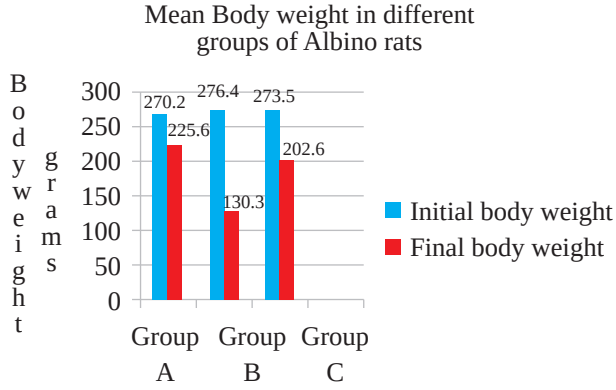
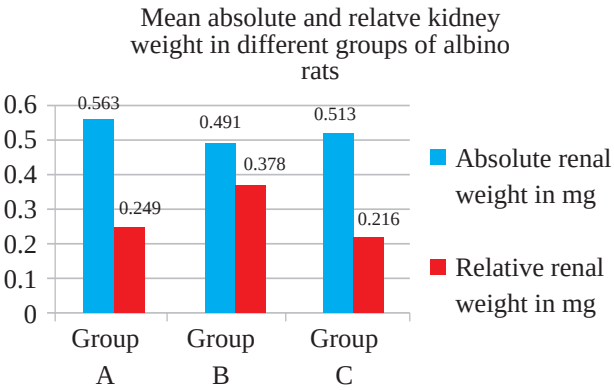


Table-3



DISCUSSION:

Different approaches have been planned to reduce diabetes-induced nephrotoxicity. L-arginine, a nitric oxide precursor, is found to exert a protective effect and improves renal functions in various forms of acute and chronic renal injury.[16]

In the present study, we have investigated the ability of L-arginine to prevent STZ-induced nephrotoxicity. Streptozotocin administration to rats increased blood glucose. L arginine-treated streptozotocin-diabetic rats exhibited a decrease in plasma glucose. L-arginine by its ability to scavange free radicals and to inhibit lipid peroxidation, prevents streptozotocin-induced oxidative stress and protects ß-cells resulting in increased insulin secretion and decreased blood glucose levels.[17] Studies have proved that L-arginine has protective effect on renal hypertrophy induced by STZ-treatment.

Hyperglycemia due to STZ result in nephrotoxicity.[18] STZ induced hyperglycemia caused increase in both absolute and relative renal weight.[19] Studies have proved long term consequences of high glucose levels on the morphology and function of different cell types.[20] This finding was in agreement to the present study. The increase in the absolute weight of kidney was due to hypertrophy of the organ.[21] Whereas, the relative renal weight gain was affected by the total body weight loss. Many reports demonstrated the inhibitory effect of exogenous NO on the nephrotoxicity.[22] This observation was in accordance with the present study demonstrating the significance of L-arginine in reducing the severity of renal damage in animals exposed to nephrotoxic drugs like STZ.[23,24] Group B animals given STZ showed marked body weight reduction.[25] There was an increase in absolute and relative renal weight which was due to STZ induced hyperglycemia.[26]

In Group C L-arginine was used to reverse the damage by STZ induced hyperglycemia; it also prevented absolute and relative renal weight gain. The ability of L-arginine to reduce the body weight loss resulted from increase in skeletal muscle protein synthesis and reduction of skeletal muscle protein degradation.[24]

CONCLUSION:

L-arginine as nitric oxide donor and antioxidant plays substantial role in preventing body weight loss and preserving renal morphology in STZ-treated hyperglycemic experimental animals. Further experimental and clinical studies are required before L-arginine could be used as a supplement for the treatment of diabetes mellitus and its complications.

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ORIGINAL ARTICLE

Foeto-Maternal Outcome Of Abruptio Placentae at a Tertiary Care Hospital

Shazia Naseeb[1], Shoaib Malik[2], Haleema Yasmin[3], Razia Korejo[4]

ABSTRACT:
Objective: To determine the frequency, risk factors and, maternal and perinatal outcome in women presenting with abruptio placentae at a tertiary care hospital.
Methodology: This observational, descriptive study was conducted in the Department of Obstetrics and Gynecology Unit I, Jinnah Postgraduate Medical Centre (JPMC), Karachi from January 2011 to December 2013. All pregnant women with gestational age 28 weeks or greater, having retro-placental clots on ultrasound and/or painful vaginal bleeding were included by using non-probability purposive sampling technique.
Results: There were 24,591 obstetric admissions during the study period, and 21,669 of them delivered. Of these 489 were diagnosed as abruptio placentae, making it a condition with a frequency of 1.98% of obstetric admissions and 2.25% of deliveries. 394 of the 489 cases (80.6%) were un-booked. Majority of them (252, 51.5%) were grand multipara with mean parity of 4.8 ± 3.3. 330 (61.4%) were older than 30 years (36.1± 12.6 years). 392 (80.2%) delivered vaginally and the rest 97 (19.8%) were delivered by Caesarean section. Hypertension and pre-eclampsia were collectively seen in 124 (25.2%), anaemia in 77 (15.7%), smoking in 39 (7.9%) and trauma in 8 (1.6%) patients. Noteworthy maternal complications were postpartum haemorrhage (PPH) in 70 (14.3%), postpartum anemia in 55 (11.2%), disseminated intravascular coagulation in 13 (2.65%) and renal failure in 2 (0.4%) patients. Maternal death occurred in 17 (3.5%) women. Still birth occurred in 194 (39.7%) patients. Perinatal Mortality was 68.7%.
Conclusion: Abruptio placenta has a significantly increased risk of maternal and perinatal mortality. Risk factors include multiparity, hypertension, pre-eclampsia, anaemia and smoking.
Keywords: Abruptio placentae, Postpartum haemorrhage, Anaemia, Disseminated intravascular coagulation, Perinatal mortality, Maternal mortality.

Introduction:
Abruptio placenta is defined as the premature separation of a normally implanted placenta between 24-week gestation and delivery.[1] It complicates about 1% of pregnancies worldwide and 7% in Pakistan, and is a leading cause of vaginal bleeding in the latter half of pregnancy.[2,3] It is also an important cause of perinatal mortality and morbidity. The maternal effect of abruption depends primarily on its severity, whereas effect on the foetus is determined both by its severity and the gestational age at which is occurs. Exact etiologyof placental abruption remains unknown, however multiple risk factors have been identified, among which one or more may be present at a time.[4] These include maternal hypertension, pregnancy-induced hypertension, advanced maternal age, multiparity, anaemia, low socio-economic condition, trauma and smoking.[2,4,5,6] Hypertensive state of pregnancy is associated with 2.5% to17.9% incidence of placental separation.[7] Woman with HELLP syndrome have an increased risk of placental abruption.[8] Abruptio placentae can cause a number of maternal and foetal complications, which include haemorrhagic shock, disseminated intravascular coagulation (DIC), renal failure, necrotic ischemia of organs like liver, adrenal or pituitary, postpartum haemorrhage, postpartum anemia, foetal hypoxia, premature birth and intrauterine foetal demise.[2,3,6,7] Maternal complications increase in severity when women are admitted with severe abruption and intrauterine foetal death.[9,10]
This study was carried out to determine the frequency, risk factors and, maternal and foetal complications of abruptio placentae at a tertiary care public hospital.

✉ **Dr. Shazia Naseeb**
Assistant professor
Department of Obstetrics & Gynecology
JPMC, Karachi
✉ **Dr. Shoaib Malik**
Assistant professor
JPMC, Karachi
✉ **Dr. Haleema Yasmin**
Professor
Department of Obstetrics & Gynecology
JPMC, Karachi
✉ **Dr. Razia Korejo**
Professor
Department of Obstetrics & Gynecology
Bahria University Medical and Dental College
Karachi
Email: drsam222@yahoo.com
Received: 25-10-2016
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METHODOLOGY:
This descriptive observational study was conducted in the Department of Obstetrics and Gynecology unit-I JPMC, karachi from January 2011 to December 2013. During the study period, total 24,591 pregnant women were admitted, 21669 deliveries occurred and among them 489 cases of abruptio placentae were observed. All the pregnant women with gestational age 28 weeks or more with painful vaginal bleeding and/or retroplacental clot on ultrasound were included in this study by using non-probability purposive sampling technique. Women presenting with vaginal bleeding due to other causes than abruptio placenta were excluded from the study.
Patients with placental abruption were managed as an

emergency. Intravenous lines were setup, hypovolaemia was treated immediately with plasma expander and then with cross-matched blood when it became available. Following this the patients were carefully evaluated by rapid history, clinical examination, laboratory investigations and ultrasound scans.

Expeditious delivery was the mainstay of treatment and the cases of intrauterine death were preferably delivered vaginally, except in few cases where excessive bleeding necessitated abdominal route of delivery. Caesarean section was done in cases of foetal distress which was evident by non-reassuring cardiotocography(CTG). Patients who developed postpartum haemorrhage secondary to abruptio placenta were managed promptly. Uterine atony was managed by uterine massage, rectal misoprostol, oxytocic infusion and intramyometrial Prostaglandin F2-α. Patients not responding to these measures were treated by obstetrical hysterectomy. Cases with oliguria due to massive haemorrhage were treated with judicious intravenous fluid replacement and strict intake and output monitoring. Consumptive coagulopathy was treated with blood transfusion; fresh frozen plasma transfusion and patient were shifted to intensive care unit for further management. Maternal complications like shock, coagulopathy, renal failure, postpartum hemorrhage, postpartum anaemia and maternal deaths were recorded. Intrauterine, intrapartum and early neonatal deaths were looked into. Mean with standard deviation was calculated for quantitative variables like age, parity and gestational age. Frequency and percentage was computed for qualitative variables including smoking, hypertension, socio-economic status and maternal outcome or complications such as DIC, acute renal failure, shock, PPH, postpartum infection, postpartum anaemia and maternal death. SPSS-10 was used to analyze data.

RESULTS:

During the study period, total 24591pregnant women were admitted, out of which 21669 were delivered. 489 cases of abruptio placenta were observed,making the Frequency 1.98% of total admissions and 2.25% of total deliveries. Among these 489 cases, 394 (80.6%) were un-booked. Of the deliveries, 392 (80.2%) were vaginal and the rest i.e. 97 (19.8%) underwent operative delivery. In this study the most frequent age group was >30 years (300, 61.4%) with mean age of 36.1 ±12.6 years. Majority (252, 51.5%) were grandmultiparous with mean parity of 4.8±3.3. Most of the women, 265(54.2%) presented at a gestational age of more than 37-week (Table-1). Risk factors associated with abruptio placentae are shown in Table-2 whereas maternal and perinatal outcomes are detailed in Table-3.

Table-1
Maternal characteristics

	Number	% (95% Confidence Interval)
Booking Status		
Booked	95	19.4 (16.1 - 23.1)
Un-booked	394	80.6 (76.9 - 83.9)
x^2=365.6, p=0.001		
Age (Years) (36.1 ± 12.6) years		
15 – 20	78	15.9 (12.9 - 19.4)
21 – 30	111	22.7 (19.1 - 26.5)
31 – 40	111	22.7 (19.1 - 26.5)
> 40	189	38.7 (34.4 - 43.0)
x^2=72.7, p=0.001		
Parity (4.8 ± 3.3)		
0 + 0	90	18.4 (15.1 - 22.0)
1 - 4	147	30.1 (26.1 - 34.2)
5 & above	252	51.5 (47.1 - 55.9)
x^2=124.2, p=0.001		
Gestational Age (Weeks) (35.5 ± 3.2)		
28 – 36	224	45.8 (41.4 - 50.2)
37 – 40	265	54.2 (49.7 - 58.5)
x^2=6.8, p=0.008		
Mode of deliveries		
Spontaneous vaginal delivery	302	61.8 (57.3 - 66.0)
Instrumental delivery	90	18.4 (15.1 - 22.1)
Caesarian Section	85	17.4 (14.2 - 20.9)
Obstetrical hysterectomy	12	2.4 (1.3 - 4.1)
x^2=511.44, p=0.001		

Table-2
Maternal Risk Factors

Risk factors	Number	% (95% Confidence Interval)
Chronic Hypertension	85	17.3 (14.2 - 20.9)
Anemia	77	15.7 (12.7 - 19.1)
Pre-eclampsia	39	7.9 (5.8 - 10.6)
Smoking	39	7.9 (5.8 - 10.6)
Trauma	8	1.6 (0.7 - 3.0)
Polyhydramnios	5	1.0 (0.3 - 2)
x^2=145.78, p=0.001		

Table:3
Maternal & Perinatal Outcome

Maternal Complications	Number	% (95% Confidence Interval)
Hypovolemic Shock	72	14.7 (11.8 - 18.0)
PPH	70	14.3 (11.4 - 17.6)
Postpartum Anemia	55	11.2 (8.6 - 14.2)
DIC	13	2.65 (1.4 - 4.4)
Renal Failure	2	0.4 (0.06 - 1.3)
Maternal Deaths	17	3.5 (2.1 -5.4)
x^2= 137.29, p=0.001		
Perinatal Outcome		
Alive	295	60.3 (56.0 - 64.6)
Still births	194	39.7 (35.4 44.0)
Early Neonatal Deaths	142	29.0 (25.1 - 33.2)
Perinatal deaths	336	68.7 (64.5 - 72.7)
x^2= 195.92, p=0.001		

DISCUSSION:

In this study the frequency of abruptio placentae was 2.25%. Clinical studies from developed countries report incidence of abruptio placentae from 0.7% to 1%.[8,9,10] In contrast, studies from developing countries report its incidence up to 7%.[11,12,13] The frequency in this study was comparable with other studies from Pakistan[14,15]. The high rate (80.6%) of un-booked cases observed in this study was also comparable with the other studies nationwide.[14,15,16] Unawareness and ignorance of antenatal care was one of the most important factors that gave way to abruptio placenta. In the developed world, the concept of un-booked cases barely existed; hence this variable was not even mentioned in studies from those parts of the world. The most frequent age group was older than 30-years. Few studies have reported a positive association of abruptio placenta with advanced maternal age[17,18] while other studies found no relationship.[19,20] Multiparity was another risk factor noted in many studies.[11,19,20] In this study grand-multiparity was noted as a predisposing factor for abruption. Most cases of abruptio placenta (52.4%) were seen at gestational age greater than 37-weeks. Others have shown either no relationship of the condition with gestational age[1] or even it being more common in preterm pregnancies. Hypertension, anemia, and smoking were other major risk factors in this study in this order. Other studies also supported our results and mention them as major risk factors for abruption in more or less similar order.[22,23,24] However, in studies from the western countries, smoking was higher in the order as it is far more frequent in their society whereas the trend of smoking in women of our population is minimal because it is not considered favorably by family and society.[27,28]

Maternal complications encountered were hypovolemic shock (14.7%), PPH 14.3%, postpartum anemia (11.2%), DIC (2.65%) and renal failure (0.4%). International as well as local studies have also reported these maternal outcomes in more or less similar proportion.[9,10,20,23,24,25] Maternal mortality was seen in 17 (3.5%) patients which was lower than another study by Mustafa 8.5%[3]. In other studies, no maternal death was reported.[26] Anemia and DIC were the major causes of maternal deaths. The women who died were admitted in hypovolemic shock and could not be revived in spite of all resuscitative measures.

Perinatal mortality (68.7%) was higher than studies from the developed world .[9,27,28] A similarly high perinatal mortality has been reported from other developing countries .[23,25,26] Nearly a third, i.e. 194 (39.7%) babies were stillborn, 295 (60.3%) babies were born alive, but 142 of them died in first 7 days of life. Follow-up of

babies in late neonatal period was not possible therefore, only early neonatal deaths were included in this study. The likely reason for high perinatal mortality was that most of the patients came very late and had intrauterine death at the time of admission, or had such severe abruption that the newborns were born in a moribund state. Abruption was not only an independent risk factor for poor outcome among babies born before 32 weeks of gestation, but a premature delivery can also increase the foetal mortality and morbidity in cases of abruption.[9, 27, 28]

CONCLUSION:

Abruptio placenta, with its high frequency, is still one of the major threats to the well-being of pregnant women in our population. Hypertension, anemia, grand multiparity and smoking are its major risk factors. Major adverse maternal outcomes are postpartum anemia, hypovolemic shock, postpartum haemorrhage and maternal death. Abruptio placenta can also result in significant perinatal morbidity and mortality.

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ORIGINAL ARTICLE

Correlation of the Camper Planes with Respect to Occlusal Plane in Prosthodontic Rehabilitation

Muhammad Haseeb Rana[1], Gotam Das[2], Naveed Innayat[3], Nadia Munir[4], Khawaja Rashid Hassan[5]

ABSTRACT:

Objective: To measure the mean camper planes I, II and III with reference to the occlusal plane to determine the smallest angle in Prosthodontic rehabilitation.

Methodology: This study was carried out in the department of Prosthodontics, de' Montmorency College of Dentistry and Punjab Dental Hospital, Lahore from 19th May to 18th November 2012. Total 50 patients were included. Cephalometric radiographs were taken. On Cephalogram angles were measured between Camper's I, II, and III with occlusal plane. All measurements were calculated and data analysis was done by using SPSS version 17.

Result: Mean Camper plane I-OP was $1.67^0 \pm 0.94$, Camper plane II-OP was $2.60^0 \pm 1.07$ and mean for Camper plane III-OP was $3.60^o \pm 1.19$.

Conclusion: According to this study, angle between Camper's I (superior border of the tragus to the lowest point of ala) was most precise in orienting the occlusal plane.

Key words: Camper's Plane, Occlusal Plane, Prosthodontic Rehabilitation.

INTRODUCTION:

The occlusal plane is established by the incisal and occlusal surfaces of the teeth. The inclination of the occlusal plane is one of the key factors governing occlusal balance, function, aesthetics and stability of the prosthesis in prosthodontic rehabilitation.[1-3] The failure to reproduce the occlusal plane can jeopardize the interaction between the tongue and the buccinator muscle.[4] The most widely used method in determining the occlusal plane is the camper's plane as a reference point.[5]

There is controversy in determining camper's plane. Spratley, Boucher, Neill and Naim claim that camper's line runs from the center of the ala of the nose to the center of the tragus of the ear[5]. Glossary of Prosthodontic Terms[6] states that the Camper's line runs from the inferior border of the ala of the nose to the superior border of the tragus of the ear. Lundström[7] measured camper's I, II, III with the occlusal plane. Camper I was formed from the superior border of the tragus of the ear to the lowest point of the ala of the nose. Camper II was formed from the middle border of the tragus of the ear to the lowest point of the ala of the nose. Camper III was formed from the inferior border of the tragus of the ear to the lowest point of the ala of the nose. They found that the mean value of camper I was 2.06°±2.1°, camper II was 3.15°±1.6° and camper III was 6.1°±1.6°. This study showed that the angle between occlusal plane and camper I was more accurate and the differences between the three planes in relation to the occlusal plane were significant ($p < 0.001$)[5]. Another study conducted in 2009 concluded that the magnitude of Camper's I was 1.801°±3.123 Camper's II was 4.160°±3.893 and Camper's III was 5.839°±4.770[2].

The aim of this study was to determine the mean Camper's plane I, II, III as a guide for the orientation of the occlusal plane in prosthodontic rehabilitation. Use of cephalometric landmarks on dentate individuals to measure the occlusal plane was done in relation with Camper's I, II, III planes. This study could provide a guide line that which plane should be used for the orientation of occlusal plane on edentulous patient for their better management and to achieve more patient satisfaction.

METHODOLOGY:

A total of 50 subjects, fulfilling the inclusion criteria were enrolled.The radiographs of subjects having 28 to 32 teeth of either gender, with Angle's class I molar relationship assessed on visual bases, were selected from the department of Prosthodontics of de' Montmorency College of Dentistry and Punjab Dental Hospital, Lahore from 19th May 2012 to 18th November 2012. An informed consent was taken from every subject. A cephalometric radiograph was taken in standing position for each subject, using an orthopantomograph model Orthophos-5 (Siemens) with a focal film distance of 5 feet. Subjects were asked to close in centric

Dr. Muhammad Haseeb Rana
Assistant Professor
Department of Prosthodontics
Islam Medical & Dental College,
Sialkot.
E-mail: haseeb_rana1@hotmail.com

Dr. Gotam Das
Assistant Professor
Department of Prosthodontics
Bhitai Dental & Medical College,
Mirpurkhas

Dr. Naveed Innayat
AssistantProfessor
Department of Prosthodontics
Islam Medical & Dental College,
Sialkot.

Dr. Nadia Munir
Assistant Professor
Islam Medical & Dental College
Sialkot

Dr. Khawaja Rashid Hassan
Assistant Professor
Department of Dental Materials
Islam Medical & Dental College,
Sialkot.

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occlusion. Using cephalostat the patient's head was fixed bilaterally by the ear rods and anteriorly by a plastic stopper on the bridge of the nose. The cassette with the film inside was at the right side of the patient's face. Radiographs were obtained at 66 to 69 kVp and 15 to 16 mA according to individual's status. Kodak T-MAT films with Siemens special screens were used for conventional cephalometric radiography. Barium sulfate creamy mix was applied to the teeth; one drop on the incisal edge of the left central incisor, another drop was painted to cover the mesio-palatal cusp of the left first molar. Another creamy mix of barium sulfate was painted on the skin on the left side of each subject's face in the shape of a triangle to mark required landmarks to be shown in the final radiograph. The apex of the triangle was superiorly pointed to the lower border of the ala of the nose, and the other one was applied to mark the whole tragus of the ear. The apex of the painted triangle of the tragus was pointed posteriorly to the tragus so that the lowest angle between occlusal plane and ala tragus line at the superior, middle and inferior border of the tragus would be identified.

Each traced cephalogram was placed on the conventional viewing box, measuring the angles between Campers's I, II, III with occlusal plane. All measurements were calculated by researcher himself. All this information was recorded on proforma.

SPSS software version 17.0 was used to calculate the mean and standard deviation of all angular measurements of Camper's I, Camper's II, Camper's III and age for the whole sample. Frequency and percentage was calculated for qualitative variables like gender.

RESULTS:

Mean age of the patients was 30.26±1.45 years. Age of patients was also presented in relation to gender (Table-1). Gender distribution of the patients showed that there were 48% female and 52% patients were male (Figure-1). Mean Camper plane I-OP was 1.67^0±0.94. Minimum and maximum Camper planes I-OP was 0^0 and 4^0 respectively. Mean Camper plane I-OP in male and female patients was 1.82^0±0.93 and 1.50^0±0.94 respectively (Table-2). Average Camper planes II-OP was 2.60^0±1.07. Minimum and maximum Camper planes II-OP was 1^0 and 4.50^0. Average Camper planes II-OP in male and female patients was 2.76^0±1.04 and 2.41^0±1.10 respectively (Table-3). Mean for Camper planes III-OP was 3.60^o±1.19. Maximum and minimum Camper planes III-OP was 5.50^o and 1.50^o respectively. In female patients mean Camper plane III-OP was 3.37^o±1.22 and in male patients mean Camper planes III-OP was 3.80^o±1.14 respectively (Table-4).

Figure: 1
Gender Distribution of Patients

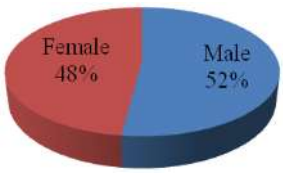

Table:1
Descriptive Statistics for Age in Relation to Gender

	Male	Female	Total
n	26	24	50
Mean	30.84	29.62	30.26
Std. Deviation	1.22	1.43	1.45

Table: 2
Descriptive statistics for camper plane-I with reference to occlusal plane

	Male	Female	Total
n	26	24	50
Mean	1.82	1.50	1.67
Std. Deviation	0.93	0.94	0.94
Minimum	0.00	0.50	0.00
Maximum	3.00	4.00	4.00

Table: 3
Descriptive statistics for camper plane-II with reference to occlusal plane

	Male	Female	Total
n	26	24	50
Mean	2.76	2.41	2.60
Std. Deviation	1.04	1.10	1.07
Minimum	1.00	1.00	1.00
Maximum	4.00	4.50	4.50

Table: 4
Descriptive statistics for camper plane-III with reference to occlusal plane

	Male	Female	Total
n	26	24	50
Mean	3.80	3.37	3.60
Std. Deviation	1.14	1.22	1.19
Minimum	1.50	1.50	1.50
Maximum	5.50	5.00	5.50

DISCUSSION:

The occlusal plane (OP) is important in dentistry, but is difficult to determine exactly in the edentulous patient. An erroneous orientation of the OP may result in tongue and cheek biting, or food accumulation in the sulcus and instability of the dentures.[8,9,10,11-17]

Extraoral landmarks that have been suggested to orient the OP are the interpupillary line, and Camper's line or ala-tragus line (ATL). Commonly used intraoral landmarks are the lips and the commissures, residual ridges, retromolar pad, hamular notch incisive papilla plane, lateral borders of the tongue and the buccinator grooves. While Nissan, Barnea, Zeltzer and Cardash suggest to consider intraoral structures during OP determination, Spratley believes that the intraoral landmarks are valuable guides for the experienced clinicians but they are rather difficult to follow.[11,15,17,18,19,20]

Although the technique for using the ATL is well

documented, there is some controversy over whether to take the superior border, the tip, or the inferior border of the tragus of the ear as posterior reference points to define ATL.[10] Ismail and Bowman compared the use of an ala-tragus line oriented to the middle of the tragus with the occlusal plane of natural teeth, and concluded that dentures constructed accordingly would have an occlusal plane set far too low posteriorly. This is contradicted with current study.[9,16,21,22] Nissan et al.[23] on the other hand, recorded the angle formed between occlusal plane and Camper's line as 7.08°. Abrahams and Carey[16] reported the angle formed between the natural occlusal plane and Camper's plane to be 9.66°. Augsburger[24] found the angle of the occlusal plane deviated from Camper's plane by 3.2°-7.85° in dentate patients of different facial types. (Van Niekerk[26] recorded a 2.45° angle between the occlusal plane of the complete denture and the ala-tragus line). Karkazis and Polyzois[25] did not find a correlation between Camper's plane and the occlusal plane of natural teeth (average 2.84°) or artificial teeth (average 3.25°); however, the inclination of the occlusal plane on complete dentures was similar to the natural occlusal plane. The difference between the average angle (2.0°) made by the occlusal plane and Camper's plane as found in the present study and that of other studies can be explained by the use of different points of measurement. Van Niekerk et al.[26] used the inferior border of the tragus as the posterior border of the ala-tragus line, whereas Karkazis and Polyzois used the center of the tragus as the posterior border of Camper's plane.[25] Results reported by another study[5] showed that Angle between occlusal plane in the dentate group and Camper's I was 2.063°±2.11, between OP and Camper's II, was 3.15°±1.63 and angle between OP and Camper's III was 6.12°±1.65 respectively. They demonstrated that the superior border of the tragus is the most acceptable point to orient the occlusal plane, which complies with Boucher, the Glossary of Prosthodontic Terms. On the other hand, these results do not agree with the findings of other study.[25] who had suggested the use of the inferior part of the tragus rather than middle or superior, while Ismail and Bowman[9] suggested the use of the middle part of the tragus. From the results of this study, it can be inferred that use of the Camper's plane I may be clinically a useful reference line for the initial orientation of the OP, but it should be taken only as an approximation. Final determination of it is governed by other criteria like intra-oral land marks. If used, it would seem preferable to define it as running from the inferior border of the ala of the nose to the tip or to the superior border of the tragus of the ear.

CONCLUSION:

According to the results obtained, angle between Camper's I (superior border of the tragus to the lowest point of ala) was most precise in orienting the occlusal plane in prosthodontic rehabilitation.

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ORIGINAL ARTICLE

Effect of Altered Sleep Rhythm on Body Mass Index

Surriya Jabeen

ABSTRACT:

Objective: To assess the influence of de-synchronized sleep rhythm caused by rotatory shift work on Body Mass Index (BMI) in health care providers.

Methodology: This cross-sectional study was conducted in Dow university hospital Karachi, from November 2013 to May 2015. To outline underlying risk factor for obesity, a universal sample of all eligible health care providers working in split shifts (service across 24 hours of the clock, each day of the week)(n=91) were enlisted. We used the BMI calculator of heart foundation Australia. However, Asian cutoff points by WHO were also taken into consideration (BMI classification Global data base on BMI, WHO 2006) whereby BMI above 25 was considered to be obese in the Asian countries (WPRO criteria). BMI was determined by using metric system. Height was recorded in centimeters and weight was obtained in kilograms. Gender based BMI was calculated for adult men and women. The healthy range of BMI was 18.5-25. Exclusion criteria included pregnant women, age less than 18 years and chronic illness.

Results: Results revealed an increased BMI amongst the shift workers. However, female health care providers far outnumber the male health care providers as it was observed that 16 women (43.2%) were found to have BMI more than 25 as compared to 9 (16.7%) men.

Conclusion: Split shift work was identified as independent risk factor for obesity. Identification of irregular sleep cycle as an underlying mechanism leading to obesity necessitates further evaluation.

Keywords: Sleep, Obesity, Body mass index, Split shift work,Weight gain

INTRODUCTION:

Diseases are now considered to be multifactorial in origin. Mere presence of one factor is not sufficient to initiate a disease process.Currently there is a growing interest in job-related trauma; one such risk factor is working in irregular timings. Sleep wake timing in the human body is controlled by a complex interplay of a biological clock regulating the transition between dark and light cycle (day/night). Sleep rhythm is uniform in all human beings, which is maintained by the endogenous clock. Suprachiasmatic nucleus in the anterior hypothalamus plays a major role besides the peripheral oscillators in the organs.[1] Sleep cycle (Day/Night) of an individual which maintains body hemostasis results in a state when body metabolic pathways are operational and oscillating to storage pathways during sleep. However, this alternate swing between storage, metabolism and overnight fast are regulated by certain hormones namely insulin/ Glucagon ratio, which in turn is influenced by day and night oscillation; this sleep wake time are distressed due to rotatory/split shift work.[2]

Obesity has now become a pandemic dilemma, according to WHO, obesity is the most overlooked public health problem.[3] It is currently a worldwide challenge, having multiple determinants, nevertheless job related factors are drawing major attention from research community. The prevalence of elevated body mass index and obesity in several Asian countries is about 3.0%.[4] The computer age has led to many changes in life style; several workers are now working online in night shifts, students with part-time jobs, 24-hours-economy,video-game shops, all have influenced daily life at the expense of sleep shape.The perfunctory glance illustrates the complexity of changed life-style and behavioral cycle that has been found to be variably associated with the change in disease pattern. Rotatory shift workers are frequently found to be obese. Multiple studies have linked linear association between short sleep duration and weight gain. It was observed that increased intake and decreased energy utilization seen in split sleep pattern as in irregular shift worker is one of the factor associated with weight gain.[5,6] Proximate research postulated that intentional variations to natural sleep duration effect BMI, and familial pattern did not seem to play any role.[7] Prior researches with major focus on sleep/wake parameters suggested a positive relationship between sleep cycle and obesity.[8] BMI, which stands for body mass index is a precise bench mark to draw a conclusion if the individual is normal, overweight or underweight. It is valuable because if BMI ascends or descends from the ideal range, it has a linear association with the health issues.[9] It was also witnessed that irregular shift workers were unable to participate in programmed sports and exercise which might have further contributed to elevated body mass index.[10] Chronic diseases, for instance diabetes, hypertension and cardiovascular disease now appear as new challenge which are mostly prevalent in overweight individuals.[11]

With this background, aim of the study was to assess the impact of the irregular sleep/wake oscillation on body mass index and to determine relationship between sleep configuration and obesity.

✉ **Dr. Surriya Jabeen**
Associate Professor
Department of Community Medicine
Dow International Medical College
Email:fmddimc@gmail.com
Received: 03-11-2016
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METHODOLOGY:

This was a cross-sectional study conducted between November 2013 and May2015 in Dow University Hospital Karachi. A universal sample included all health care providers working in rotatory/split shifts. Demographic characteristics including age,gender, education and vocational status was identified. Subjects exclusively working in irregular shifts who were healthy

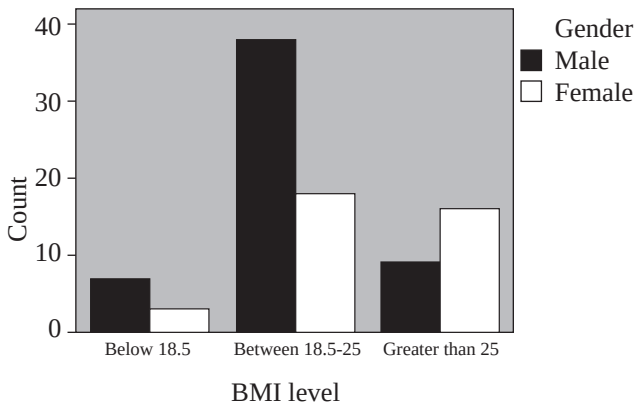
and fit to participate were included, while subjects with history of any chronic morbidity like diabetes, hypertension, nicotine use, drug abuse, mental illness, on any psychiatric treatment, pregnant women, and under 18-year-age were excluded. The study population was working 8-hour per day, and were rotated every ten days; the direction was from morning to evening-shift and finally night shift.The study was preceded by a pilot study examining 12 subjects.

Then final study was initiated after obtaining written informed consent from the enrolled subjects, and a formal written permission from the hospital management.The measuring tool was BMI calculator from Heart foundation Australia using the formula, Body weight (kg) divided by squared height (m^2). Anthropometric measurement included height and weight. Height was recorded in centimeter and weight was obtained in kilogram. Calculated BMI was split in to three categories; underweight, normal weight, and overweight, based on recommended age and gender. BMI of female and male participants was segregated. Healthy BMI range was between 18.5-25. Obesity was defined as a body mass index = 25 kg/m^2 for Asian countries(WPRO criteria), and underweight below 18.5. These categories have been proven useful measurement for most people over 18 years. All data analysis was carried out on SPSS version 20. Quantitative variables were presented by their mean ± SD while qualitative variables were presented by frequency and percentages.

RESULTS:

Participants in the current study were104; however, 91 complete data forms were received. Response rate was 87.50 %. Most of the subjects in the current study were males, 54 (59.30%), whereas female subjects were 37 (40.70%). Mean age was 27.78±5.78. The number of subjects within the healthy BMI range were 56 (61.5%), which included 38 males (70.4%), and 18 females (48.6%). The obese category comprised 25(31.9%) participants and amongst them 16 women (43.2%) and 9 (16.7%) men were included. The number of underweight subjects were 10 (13.8%) and included 3 (8.10%) females and 7 (13.0%) males (Figure-1).

Figure: 1
Graphical presentation of BMI among health care providers



DISCUSSION:

Our results did not reveal a correlation between rotatory/split shift work and increased body mass index, however, more women shift workers were observed to be overweight as compared to males shift workers. Many chronic diseases, such as Type-2 diabetes and metabolic syndrome have been known to be directly related to overweight.[12] A new window was unlocked with the introduction of graded cutoff points to determine BMI by WHO in Asian population, the objective of the cut off points was to classify on a continuum the level where the subjects should be placed on BMI scale, still BMI and those cutoff points could not correlate overweight and chronic diseases in isolation without considering other risk factors.[13] Prior research had revealed that direction of shift work and its frequency were related to negative health consequences,[14] hence, split shift work must be addressed from various perspectives including duration and frequency of night shifts.[15] Newer approach of introducing healthy shift schedule had a promising health influence.[16,17] It was observed in the current study that our subjects were mostly sleep deprived. Anthropometric measurement included height and weight. Waist to hip ratio was not included in our study since it was witnessed from prior data that waist to hip ratio might result in false inference, as waist measurement was influenced by the parity of the women.[18]

Proximate researches had published various health effect of this type of split sleep structure that could initiate unhealthy practices by the employee; de-synchronization of endogenous circadian sleep rhythm made them vulnerable for irregular meals that had further increased the chances of weight gain.[19,20] The prior researches had also evidenced that minor changes in eating habit were leading to cumulative effect.[21] The relationship between sleep deprivation and overweight dates back to sixties, when analysts indicated a link between body weight change and sleep disorders.[22] Present study was meant to further strengthen previous observation. Although mechanism of sleep architecture and weight related changes were well described in the past, however, there was scarce knowledge about the relationship between sleep and obesity. Prior research had observed that a low caloric diet might had an association with a low level of sleep-inducing gut peptide,which in turn effect the waking hormone orexin which modulates the sleep/wake cycle.[23] Previous research also observed increased prevalence of depression among split shift workers, which might in turn be responsible for increased food intake and overweight. Earlier studies had focused on depression being responsible for obesity, therefore it became necessary to identify depression as a variable when analyzing the link between split work and weight gain.[24] A recent study on Australian subjects revealed that the people with sedentary jobs were more active during free time as compared to the individuals engaged mostly in walking and heavy work occupation.[25] From sleep-wake time system perspective, human body was not meant for nocturnal eating. It was demonstrated

that feeding at night increased the LDL/HDL profile.[26] It was also observed that glucose balance descended from dawn to dusk.[27] Body clock was also evidenced to play a crucial role on plasma triglyceride level, with elevated nocturnal level which itself was an underlying risk factor for cardiovascular pathology.[28] For a long time, split shift-work had been vital to deliver essential services. Over the years man made environment has changed life style. Currently, the desynchronized environment and its interaction with man's endogenous rhythm imposed penalties to the human body. The new jobs opening in call centers, shopping malls, 24/7 banking, as well as early morning shifts have affected the life pattern of a common man. Many employees are currently working outside day light range which is not harmonized to the natural biological rhythm with in human body, thereby producing diseases like hypertension and glucose intolerance.[29] Currently irregular shift employment ranges from 13–20% in Europe and the United States. Multiple well-controlled epidemiological studies advocated irregular shift work as an independent variable of elevated BMI.[30] However, there were certain limitations in our study. The sample size was relatively small, and the subjects were from a multicultural slum area.

CONCLUSION:

Despite the limitation of the current study, it was observed that split shift work is an independent risk factor for increased BMI. Identification of irregular sleep cycle as an underlying mechanism leading to obesity necessitates further evaluation of rotatory shift on BMI in diverse geographical meridian since no data is available from this region.

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ORIGINAL ARTICLE

Prevalence of Hypertriglyceridemia and Risk Factors of Ischemic Versus Hemorrhagic Stroke

Ayaz Ahmed[1], Muhammad Fahad Waseem[2],Wajeeha Ahad[3],
Muhammad Tahir[4], Naveed Aslam[5]

ABSTRACT

Objective: To find the prevalence of hypertriglyceridemia in ischemic and hemorrhagic strokes and to assess the risk factors associated with them.

Methodology: This cross-sectional study was conducted in Medical OPD/ Emergency, PAF Hospital Mushaf, Sargodha over a period of six months from Nov-2010 to May-2011. All patients of either gender diagnosed as having stroke, with hyper dense or hypo dense area on CT scan brain and of age more than 30 years were included in the study. Patients on anti-hyperlipidemic drugs, with previous history of stroke, having blood disorders, like hemophilia and idiopathic thrombocytopenic purpura and, on warfarin therapy were excluded from the study.

Results: 203 patients were enrolled in the study. Out of these 203 patients 138(68%) were males, 65 (32%) were females. 127(62.6%) stroke patients had hypertriglyceridemia. In multivariate analysis, hypertriglyceridemia was found to be the only risk factor associated with ischemic stroke adjusting for all the other variables. It was found that patients with hypertriglyceridemia had 3.24 times higher odds of having ischemic stroke (P-value=0.017).

Conclusion: Hypertriglyceridemia was found in majority of the patients with stroke. Furthermore, it was found to be an independent risk factor of ischemic stroke.

Keywords: Ischemic stroke, Hemorrhagic stroke, Hypertriglyceridemia

INTRODUCTION:

Stroke is a medical emergency and can bring about consistent neurological disability. It is the third leading cause of functional impairment and mortality.[1-3] According to the World Health Organization (WHO) stroke results in cerebral malfunction rapidly, with symptoms continuing 24 hours or more prompting death with no apparent cause other than of vascular origin.[4] WHO anticipated stroke cases to ascend from around 38 million Disability-Adjusted Life Years (DALYs) universally in 1990 to 61 million Disability-Adjusted Life Years (DALYs) in 2020.[5] In Gulf states, yearly rate of stroke ranges from 27.6 to 57 for each 100,000 individuals with ischemic stroke being most widely recognized subtype.[6] In Pakistan the epidemiological studies on stroke is scarce. Few studies done on this subject reported that its incidence in Pakistan is as low as 4.8%-6.4% and as high as 64.9%.[7-9]

Hypertriglyceridemia is a lipid anomaly with raised levels of triglycerides. Several clinical trials showed an association between high concentrations of serum cholesterol and ischemic stroke.[10,11] According to Adult Treatment Panel-III rules, serum triglyceride levels can be classified as normal less than 150 mg/dl, marginal high 150-199 mg/dl, high 200-499 mg/dl and very high more than 500 mg/dl. ATP III reported the rate of hypertriglyceridemia to be 33% globally.[12] Several studies reported multiple risk factors for stroke like age, gender, smoking, hypertension, diabetes mellitus, triglycerides, serum total and HDL cholesterol, along with hypertriglyceridemia.[13,14] Hypertriglyceridemia has been reported as an independent risk factor for ischemic stroke.[15,16] In any case, considering hypertriglyceridemia as an autonomous risk factor for ischemic stroke is still disputable and vast scale studies are required to evaluate this problem.[17,18] Keeping this background in mind, we investigated the prevalence of hypertriglyceridemia in ischemic and hemorrhagic strokes and assessed the risk factors associated with both types of stroke.

METHODOLOGY:

This cross-sectional study was conducted in Medical OPD/Emergency, PAF Hospital Mushaf, Sargodha, over a period of six months fromNovember-2010 to May-2011. All patients of either gender, diagnosed as having stroke (hyper or hypodense area) on CT scan brain and of age more than 30years were included in the study. Patients on anti-hyperlipidemic drugs, with previous history of stroke, blood disorders like hemophilia, idiopathic thrombocytopenic purpura and on warfarin therapy were excluded from the study. Fasting serum

✉ **Dr. Ayaz Ahmed**
Medical Specialist
PAF Hospital Samungli
Quetta
Email: drayazahmedpk@hotmail.com
✉ **Dr. Muhammad Fahad Waseem**
Medical Specialist
PAF Hospital Masroor
Karachi
✉ **Dr. WajeehaAhad**
Medical Specialist
PAF Hospital Korangi
Karachi
✉ **Dr. Muhammad Tahir**
Medical Specialist
CMH Rawalpindi
Rawalpindi
✉ **Dr. Naveed Aslam**
Medical Specialist
PAF Hospital
Lahore
Received: 16-11-2016
Revised: 12-12-2016
Accepted: 15-12-2016

triglycerides was sent within 24 hours of onset of symptoms of all the eligible patients. Demographic details and medical history was also taken. All the data was entered and analyzed using SPSS version 21.0. Mean (SD) was computed for all the quantitative variables. Frequency and percentage were computed for all the qualitative variables. Chi-square/Fisher-exact test/Likelihood ratio chi-square test was applied to assess significant association of various qualitative variables with stroke. Univariate and multivariate logistic regression were applied to assess associated significant risk factors. P-value < 0.05 was considered significant.

RESULTS:

A total of 203 patients were enrolled in the study. Out of these 203 patients 138(68%) were males and 65 (32%) were females. More than half of the stroke patients (62.6%) were found to have hypertriglyceridemia. Most common comorbidities reported were diabetes 63.6%, followed by hypertension 56.6% and obesity 42.8%. Majority of the patients 179 (88.2%) had ischemic stroke and 24 (11.8%) had hemorrhagic stroke (Table-1). Average age of the patients was 53.5 years (±SD:10.02). 85 (41.9%) patients were of age 51-60 years, 52 (25.6%) were of age 41-50 years, 37(18.2%) 61-70 years and 29 (14.3%) 30-40 years. No significant difference was observed in mean age of the patients between both types of stroke (P-value=0.601, Table-1). Hypertriglyceridemia, smoking and hypertension were the risk factors found to be significantly associated with both types of stroke (P-value: 0.024, 0.014 and 0.018 respectively; Table-1). Gender, family history of stroke, diabetes mellitus, and obesity were not found to be significant risk factors (Table-1). In multivariate analysis, hypertriglyceridemia was found to be the only risk factor associated with ischemic stroke adjusting for all the other variables. It was found that patients with hypertriglyceridemia had 3.24 times higher probability of having ischemic stroke (P-value=0.017, Table-2).

Table 1:
Univariate analysis of risk factors of strokes

	Type of stroke						
Risk factors	Haemorrhagic		Ischemic		Total		
	n	%	n	%	n	%	P-value
Age in years	Mean	SD	Mean	SD	Mean	SD	
	52.17	13.69	53.69	9.45	53.69	9.45	0.601
Gender							
Male	18	75%	120	67.0%	138	68.0%	
Female	6	25.0%	59	33.0%	65	32.0%	0.432
Total	24	100.0%	179	100.0%	203	100.0%	
Family history of stroke							
Yes	11	45.8%	57	31.8%	68	33.5%	
No	13	54.2%	122	68.2%	135	66.5%	0.173
Total	24	100.0%	179	100.0%	203	100.0%	
Smoking							
Yes	16	66.7%	72	40.2%	88	43.3%	
No	8	33.3%	107	59.8%	115	56.7%	0.014*
Total	24	100.0%	179	100.0%	203	100.0%	
Hypertriglyceridemia							
Yes	10	41.7%	117	65.4%	127	62.6%	
No	14	58.3%	62	34.6%	76	37.4%	0.024*
Total	24	100.0%	179	100.0%	203	100.0%	
Diabetes mellitus							
Yes	18	75.0%	111	62.0%	129	63.5%	
No	6	25.0%	68	38.0%	74	36.5%	0.214
Total	24	100.0%	179	100.0%	203	100.0%	
Hypertension							
Yes	19	79.2%	96	53.6%	115	56.7%	
No	5	20.8%	83	16.1%	88	43.3%	0.018*
Total	24	100.0%	179	100.0%	203	100.0%	
Obesity							
Yes	13	54.2%	74	41.3%	87	42.9%	
No	11	45.8%	105	58.7%	116	57.1%	0.233
Total	24	100.0%	179	100.0%	203	100.0%	

*P-value<0.05, **P-value<0.0001, ǂ Chi-square test, ǂ Independent sample T-test

Table: 2
Possible risk factors associated with ischemic stroke

Risk factors	Univariate Ischemic stroke[a]		Multivariate Ischemic stroke[a]	
	OR (95%) CI	P-value	OR (95%) CI	P-value
Age in years	1.02 (0.97 - 1.06)	0.483	1.02 (0.97 - 1.07)	0.375
Gender				
Male	0.89 (0.26 - 1.80)	0.435	0.98 (0.29 - 3.26)	0.977
Female	Ref		Ref	
Family history of stroke				
Yes	0.552 (0.23 - 1.31)	0.177	0.75 (0.25 - 2.23)	0.607
No	Ref		Ref	
Smoking				
Yes	0.336 (0.14 - 0.83)	0.018*	0.41 (0.15 - 1.13)	0.086
No	Ref		Ref	
Diabetes mellitus				
Yes	0.54 (0.21 - 1.44)	0.220	0.76 (0.26 - 2.17)	0.601
No	Ref		Ref	
Hypertension				
Yes	0.30 (1.1 - 0.85)	0.023*	0.37 (0.12 - 1.11)	0.077
No	Ref		Ref	
Obesity				
Yes	0.59 (0.25 - 1.40)	0.237	0.79 (0.28 - 2.25)	0.660
No	Ref		Ref	
Hypertriglyceridemia				
Yes	2.64 (1.11 - 6.29)	0.028*	3.24 (1.24 - 8.47)	0.017*
No	Ref		Ref	

a: Reference category is hemorrhage stroke; *P-value<0.05, **P-value<0.0001, Binary logistic regression

DISCUSSION:

Association of serum triglyceride concentration with risk of stroke is well known. A few studies showed negative results while others demonstrated a positive relationship with high serum triglyceride concentration[19]. A previous study established a direct relationship between serum triglyceride level and non-hemorrhagic stroke, while no affiliation was found of high plasma triglyceride concentration as a risk factor for both types of stroke.[19,20] In this study, we found that the incidence of ischemic stroke was higher than that of hemorrhagic stroke. The results of this study suggested that the factor of advanced age was of similar importance to both types of stroke. Ischemic stroke was found to be prevalent in men, patients with family history of stroke, diabetics, and obese patients but the results were not statistically significant.

Previous studies revealed that hypertension was the most important autonomous risk factor for both ischemic and hemorrhagic stroke, and that in 50%-60% of patients, stroke was triggered by hypertension[21]. Variable risk factors of stroke include hypertension, diabetes mellitus, atrial fibrillation, dyslipidemia and hyperfibrinogenemia.[22] In our study, hypertension and smoking were not found to be the risk factors for ischemic stroke; however, both were associated with hemorrhagic stroke. Antonios et al. reported hypertriglyceridemia as an independent possible risk factor for ischemic stroke [17,24]. Our study also supported this result. In this study, hypertriglyceridemia was found to be the only possible risk factor associated with ischemic stroke in the multivariate analysis adjusting for age, gender, family history of stroke, diabetes mellitus, smoking, hypertension and obesity[14,23,24,25]. The results showed that patients with hypertriglyceridemia had 3.2 times higher odds of having ischemic stroke.

The limitation of this study is less number of patients with hemorrhagic stroke that might be a cause of insignificant results of various important variables and we also did not study other lipid abnormalities that might be the latent risk factors.

CONCLUSION:

Hypertriglyceridemia was found in majority of the patients with stroke. Furthermore, it was found to be an independent risk factor for ischemic stroke. We recommend studies to be conducted on larger scale enrolling similar number of both ischemic and hemorrhagic stroke patients; and study all the lipid abnormalities along with other risk factors.

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ORIGINAL ARTICLE

Expression of Cyclin D1 in Hyperplastic and Neoplastic Endometrial Lesions

Summayya Shawana[1], Saleha Masood[2], Zamir Ali Siddiqui[3]

ABSTRACT:
Objective: To observe and evaluate the expression of Cyclin D1 in hyperplastic and neoplastic endometrial lesions.
Methodology: This .retrospective analytical study was conducted at BMSI, JPMC over a five year period i.e. from 1-1-2008 to 31-1-2012 and was based on the analysis of endometrial samples comprising of hysterectomies and curettage. 55 endometrial samples including 25 malignant endometrial lesions, 6 complex hyperplasia with atypia, 14 complex hyperplasia without atypia, 6 simple hyperplasia without atypia, and 4 normal proliferative endometrium were analyzed for results of immunohistochemical staining.
Results: 44% (11 out of 25) cases of malignant endometrial lesions showed Cyclin D1 over expression. 66.66% (4 out of 6) cases of endometrial hyperplasia with atypia and 50% (7 out of 14) cases of endometrial hyperplasia without atypia showed Cyclin D1 overexpression.
Conclusion: Cyclin D1 overexpression was seen in a significant number of well differentiated endometrial adenocarcinomas and complex hyperplasia with atypia suggesting it to be an early event in endometrial carcinogenesis.
Keywords: Endometrial carcinoma, Hyperplasia, Cyclin D1 overexpression, Atypia, Early event.

INTRODUCTION:

Endometrial carcinoma is one of the most common malignancies of the female genital tract.[1] 7,406 new cases of endometrial cancers are registered in the UK, 88,068 in the European Union and 40,102 in North America every year.[2] According to the Shaukat Khanum Cancer Hospital & Research Centre collective cancer registry report (1994-2011), malignancies of the corpus uteri comprised 3.02% of all neoplasms in adult females.[3] Endometrial carcinomas have been classified as type1 and type 2 tumors on the basis of light microscopic appearance and clinical behavior. Endometrial hyperplasia usually precedes type 1 or endometroid endometrial carcinomas. A prolonged unopposed estrogen exposure is seen to confer a 2-10 fold increased risk for endometrial carcinoma.[4] Endometrial hyperplasia have been classified according to two systems: the WHO system and the more recent EIN system.[5,6] The WHO classification comprises of four categories: simple hyperplasia, complex hyperplasia, simple hyperplasia with atypia and complex hyperplasia with atypia. The EH-EIN-CA classification was developed by the "The Endometrial Collaborative Group" and it proposes terms endometrial hyperplasia, endometrial intraepithelial neoplasia and adenocarcinoma. The terms "Endometrial hyperplasia" (EH) or "Benign Endometrial Hyperplasia" apply to diffuse architectural and proliferative changes due to excess estrogen stimulation. EIN has been defined as a clonal proliferation of architecturally and cytologically altered premalignant endometrial glands which are prone to malignant transformation to endometroid (type 1) endometrial carcinoma. Mutations of different genes like PTEN, K-ras, Cyclin D1 and â-catenin genes and microsatellite instability along with others are the common genetic alterations observed in cases of endometrial carcinoma. Cyclin D1, a member of the cyclin G1 family, controls the transition from G1 to S phase in the cell cycle. The gene for Cyclin D1, CCND1, is a proto-oncogene localized on chromosome 11q13.[7] Cyclin D1 acts as a cell cycle promoter by binding with cyclin dependent kinases 4 and 6 (CDK4/6) and phosphorylating the retinoblastoma tumor suppressor gene. This results in the release of Rb-bound E2F members and the subsequent expression of genes required for entry into the S-phase. Further studies have shown Cyclin D1 to be an important cofactor for several transcription factors. This function of Cyclin D1 is independent of its CDK activity.[8,9] Cyclin D1 overexpression has been observed as a potential biomarker for precancerous and cancerous endometrial lesions,[10,11] while few studies contradict this finding.[12] However it is still to be determined whether Cyclin D1 participates in a causative or incidental manner in endometrial tumor progression.

Atypical hyperplasia is considered a potential precursor lesion for endometrial carcinomas; however it is still not clear whether hyperplasia without atypia poses a potential risk for developing into endometrial carcinoma. In case of endometrial hyperplasia without atypia the recommended treatment is cyclical progestins therapy whereas hysterectomy is the recommendation in patients with hyperplasia with atypia. Patients who are young

✉ **Dr. Summayya Shawana**
Assistant Professor
Department of Pathology
Bahria University Medical and Dental College
Karachi
Email: shawana75@yahoo.com
✉ **Dr. Saleha Masood**
Assistant Professor
Department of Pathology
Jinnah Medical and Dental College
Karachi
✉ **Dr. Zamir Ali Siddiqui**
Assistant professor
Department of Pharmacology
Poonch Medical College, Rawlakot,
AJK
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and wish to conceive, high dose progestin therapy may be considered as an alternate in cases of atypical hyperplasia.[4] Researches have been carried out worldwide to come up with methods for early diagnosis of endometrial carcinomas and premalignant endometrial lesions for proper therapeutic interventions. However limited work in Pakistan has been done in this regard, therefore it was decided to carry out a study to observe the differential expression of Cyclin D1 in different endometrial morphologies ranging from normal proliferative endometrium to endometrial cancers.

METHODOLOGY:

This retrospective analytical study was based on the analysis of endometrial samples comprising of both hysterectomies and curettage, received at the department of pathology BMSI, JPMC, Karachi over a five year period i.e. from 1-1-2008 to 31-12-2012. Over the five year study period we came across 294 endometrial lesions. These included 144 simple hyperplasia without atypia, 107 complex hyperplasia without atypia, 8 complex hyperplasia with atypia, and 35 malignant endometrial tumors. 55 samples were selected for immunohistochemical analysis. These included 25 malignant endometrial lesions, 6 complex hyperplasia with atypia, 14 complex hyperplasia without atypia, 6 simple hyperplasia without atypia and 4 normal proliferative endometrium. Sample size was calculated using the survey system sample size calculator. Poorly fixed tissue, inadequate material and samples of foreign nationals and Pakistanis living abroad for more than ten years were excluded. H&E stained slides were reviewed to confirm the diagnosis and the most representative section was used for immunohistochemical analysis. Anti-Cyclin D1, rabbit monoclonal antibody procured from Cell Marque, was used in all immunohistochemical analysis. Antigen detection was done using HiDef detection HRP polymer system kit (ready to use) procured from Cell Marque. Ductal carcinoma breast was taken as positive control for Cyclin D1. PBS substituted primary antibody for negative control. Sections of approx. 5µm were cut on to poly L-lysine coated slides and were deparafinized and rehydrated. Antigen retrieval was achieved by steamer method using citrate buffer, slides were allowed to cool for 20 minutes and were then placed in UV block for 5 minutes. Tissues were covered with primary antibody at dilution 1:50 and were incubated for 1 hour at room temperature. Slides were then incubated first with Amplifier and then with HRP polymer for 10 minutes. Chromogen was applied for 20 minutes and all the slides were counter stained with haematoxylin, dehydrated and mounted. Between each step the slides were washed with phosphate buffer solution (PBS).

The intensity of staining was graded as no nuclear staining (0), weak nuclear staining (1+), moderate nuclear staining (2+) and strong nuclear staining (3+). The extent of staining was estimated in percentage by counting at least 50 nuclei, calculating the ratio of reactive nuclei to total number of nuclei and multiplying it by 100. A score of 0 was used when less than 10% cells were positive, 10 to 30% immunoreactive cells were scored as 1, 31 to 60% positive cells were scored as 2 and more than 60% immunoreactive cells were scored as 3. After observing Cyclin D1 immunostaining in normal proliferative endometrium, strong staining in more than 30% nuclei was taken as overexpression of Cyclin D1. Data was collected on specially designed proforma. Statistical analysis was performed using SPSS version 21. Mean and standard deviation were calculated for quantitative variables while percentages and frequencies were calculated for qualitative variables.

RESULTS:

The 55 cases selected for immunohistochemical analysis, included 4 normal proliferative endometrium, 6 simple hyperplasia without atypia, 14 complex hyperplasia without atypia, 6 complex hyperplasia with atypia, and 25 malignant endometrial tumors. The 25 cases of malignant endometrial tumors included 18 well differentiated adenocarcinomas, 1 moderately differentiated endometrial carcinoma, 4 poorly differentiated carcinomas and two spindle cell tumors. Table-1 distributes different endometrial lesions according to age groups along with the mean age for every lesion. Table-2 shows the extent and intensity of nuclear staining of Cyclin D1 in different endometrial samples. 11 out of 25 cases of malignant endometrial tumors showed strong staining for Cyclin D1 with 9 cases showing strong reactivity in more than 60% of neoplastic cells while 2 showed strong reaction in more than 30% of cells. 10 cases of malignant endometrial tumors showed positive staining in less than 10% of nuclei. 4 out of 6 cases of atypical complex hyperplasia showed strong expression of Cyclin D1 with 2 cases showing expression in more than 60% of cells and 2 cases showing strong reaction in almost 50% of cells. Complex non-atypical hyperplasia showed strong nuclear staining for Cyclin D1 in 7 out of 14 cases with all 7 cases showing positive staining in more than 60% of cells. 2 out of 6 cases of simple hyperplasia without atypia showed strong nuclear staining for Cyclin D1 in more than 60% of cells. 2 out of 4 cases of normal proliferative endometrium showed moderate staining with Cyclin D1 in less than 30% of nuclei while 2 showed no staining at all. The 9 cases of malignant endometrial tumors which were negative for Cyclin D1 expression included 2 spindle cell tumors and 1 poorly differentiated adenocarcinoma.

Table-3 compares the expression of Cyclin D1 in different degrees of endometrial adenocarcinomas. 8(44.4%) out of 18 well differentiated endometrial adenocarcinomas showed strong intensity of staining for Cyclin D1 with 7 cases showing strong staining in more than 60% of cells. The only case of moderately differentiated carcinoma showed no staining at all. 3 out of the 4 cases of poorly differentiated carcinomas showed strong Cyclin D1 expression with positive staining in more than 60% of cells while one case showed no staining at all.

Table: 1
Distribution of different endometrial lesions according to age (n=294)

Lesions	Total no. of cases	(21-30) Yrs	(31– 40) Yrs	(41- 50) Yrs	(51-60) Yrs	(61-70) Yrs	> 70 Yrs	Mean (±S.D.)
Simple Hyperplasia without atypia	144	5 (3.97%)	50 (34.72%)	75 (52.08%)	7 (4.86%)	7 (4.86%)	0 (0%)	43.88(±8.09)
Complex hyperplasia without atypia	107	10 (9.343%)	51 (47.66%)	38 (35.51%)	6 (5.6%)	2 (1.86%)	0 (0%)	41.90(±8.04)
Complex hyperplasia with atypia	8	0 (0%)	1 (12.5%)	5 (62.5%)	2 (25%)	0 (0%)	0 (0%)	47.01(±8.05)
Malignant endometrial tumors	35	0 (0%)	3 (8.57%)	7 (20%)	15 (42.85%)	9 (25.71%)	1 (2.85%)	57.04(±8.08)

Table: 2
Nuclear intensity and extent of Cyclin D1 immunoreactivity in normal and hyperplastic endometrium and endometrial tumors (n=55)

Lesions	Total no. of cases	Extent*				Intensity**			
		0	1+	2+	3+	0	1+	2+	3+
Proliferative endometrium	4	2 (50%)	2 (50%)	0 (0%)	0 (0%)	2 (50%)	0 (0%)	2 (50%)	0 (0%)
Simple hyperplasia without atypia	6	1 (16.66%)	1 (16.66%)	2 (33.33%)	2 (33.33%)	1 (16.66%)	3 (50%)	0 (0%)	2 (33.33%)
Complex hyperplasia without atypia	14	0 (0%)	2 (14.28%)	4 (28.57%)	8 (32%)	0 (()%)	1 (7.14%)	6 (42.85%)	7 (50%)
Complex hyperplasia with atypia	6	0 (0%)	1 (16.66%)	3 (50%)	2 (33.33%)	0 (0%)	0 (0%)	2 (33.33%)	4 (66.66%)
Malignant Endometrial tumors	25	10 (40%)	3 (12%)	3 (12%)	9 (36%)	9 (36%)	2 (8%)	3 (12%)	11 (44%)

*Extent of reactivity (% of immunoreactive nuclei) was as follows: 0, <10%; 1+, 11-30%; 2+, 31-60%; 3+, >60%.
**Intensity of reactivity was as follows: 0, no staining; 1+, weak nuclear staining; 2+, moderate nuclear staining; 3+, strong nuclear staining

Table-3
Nuclear intensity and extent of ptenimmunoreactivity in different grades of endometrial adenocarcinomas (n=23)

Grades of adenocarcinomas	Tota no. of cases	Extent*				Intensity**			
		0	1+	2+	3+	0	1+	2+	3+
Well differentiated carcinoma	18	11 (61.11%)	0 (0%)	3 (16.66%)	4 (22.22%)	11 (61.11%)	4 (22.2%)	3 (16.66%)	0 (0%)
Moderately differentiated carcinoma	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
Poorly differentiated carcinoma	4	0 (0%)	0 (0%)	1 (25%)	3 (75%)	0 (0%)	0 (0%)	3 (75%)	1 (25%)

*Extent of reactivity (% of immunoreactive nuclei) was as follows: 0, <10%; 1+, 11-30%; 2+, 31-60%; 3+, >60%.
**Intensity of reactivity was as follows: 0, no staining; 1+, weak nuclear staining; 2+, moderate nuclear staining; 3+, strong nuclear staining

DISCUSSION:

In the present study we attempted to observe the differential expression of Cyclin D1 in different endometrial morphologies.The 35 malignant endometrial tumors included 2(5.4%) malignant spindle cell tumors, 2(5.4%) papillary serous carcinomas, 6(18.9%) poorly differentiated, 1(27%) moderately differentiated carcinoma and 24(67.5%) endometroid adenocarcinomas. The mean age for endometrial carcinomas was found to be 57 years and majority of the patients (67.5%) belonged to the 6th and 7th decade of life. In a study done at AKUH out of 86 cases of endometrial carcinomas 53(61.5%) belonged to the age range of 51 to 70 years.[13] In the present study Cyclin D1 immunostaining in >30% of nuclei was observed in 8 (44.4%) cases of endometroid endometrial carcinoma. Our findings correspond to those observed in other studies,[14,15,16] where strong expression of Cyclin D1 was seen in endometrial adenocarcinomas. The 2 papillary serous carcinomas in our study showed strong staining with Cyclin D1 in 60% of nuclei. Nishimurai et al[17] in one study showed significant correlation of Cyclin D1 over expression with low p53 expression, which is a frequently observed mutation in these tumors. Other studies[18,19] also observed positive expression of Cyclin D1 in 15% and 11.1% of non endometroid endometrial carcinomas while Balan et al[20] showed moderate to strong expression of Cyclin D1 in 2 out of 2 cases of papillary serous carcinomas. Immunohistochemistry was done on 6 cases of complex hyperplasia with atypia, out of which 66.6% i.e. 4 out of 6 showed Cyclin D1 overexpression. Similar higher figures were seen by Balan et al[20] who observed strong Cyclin D1 staining in 3 out of 3 cases of atypical hyperplasia. In cases of complex hyperplasia without atypia, 50% i.e.7 out of 14 cases of complex hyperplasia without atypia showed overexpression of Cyclin D1. These findings correspond to those quoted by Shevra et al.[21] Out of 6 cases of simple hyperplasia without atypia, 33.3%, i.e. 2, showed strong Cyclin D1 expression, corresponding to those observed by Quddus et al[22] and Liang et al,[16] who showed reactivity of Cyclin D1 in 30% cases of simple hyperplasia. Chaudhry and Bansal and Semczuk et al observed Cyclin D1 immunohisto-chemistry in none of the samples of simple hyperplasia without atypia.[23,24] On immunostaining, 2 out of 4 cases of normal proliferative endometrium showed moderate Cyclin D1 staining in less than 30% of nuclei while 2 showed no staining with Cyclin D1. Similar findings were observed by Shevra et al and Ozuysal et al.[21,25]

CONCLUSION:

Increasing Cyclin D1 expression was seen from normal proliferative endometrium to complex hyperplasia with atypia and carcinoma. This finding suggests that Cyclin D1 overexpression plays a role in endometrial carcinogenesis and could be an early event in endometrial carcinogenesis. Studies done worldwide suggest a potential role of Cyclin D1 in endometrial carcinogenesis. However it is emphasized that Cyclin D1 overexpression alone should not be the criteria for labeling a hyperplastic lesion as premalignant and should be correlated with other immunological and molecular markers.

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COMMENTARY

Biomedical Ethics and its Need

Quratul Ain Omaeer

ABSTRACT:
The history of medical ethics dates back to the time of Hippocrates. The involvement of philosophers, anthropologists, religious scholars and lawyers in the field of ethics gave birth to a new subject 'Bioethics.' After the human experimentations of World War II, other inhuman activities were carried on in which humans were merely used as guinea pigs. Therefore 'Bioethics' was evolved.The medical professionals should be informed about the problems and issues which are emerging. That is the reason why Biomedical ethics should be discussed with the students of health profession right from the beginning of their medical carrier. This will bring a change in the future health professionals.The doctors are required to act morally in addition to be skilled in their subject. If we want our students to be morally and ethically reflective upon the present day issues then it is a must to teach them and introduce them with the subject of Bioethics.

Keywords: Bioethics, Moral, Ethical, Experimentation, Rights, Health professionals

INTRODUCTION:

The history of medical ethics dates back to the time of Hippocrates. From the time of Hippocrates till the mid of 20th century the field of ethics was dealt by the doctors.[1] The involvement of philosophers, anthropologists, religious scholars and lawyers in the field of ethics gave birth to a new subject "Bioethics."[1,2] The subject evolved in U.S.A. in 1970's. The term Bioethics was first coined by an American biochemist, Van Rensselaer Potter.[3] The subject of Bioethics revolves around the study of moral conduct in the field of medicine.

The Nazis carried out fatal and lethal experimentations in World War II. Twenty doctors were involved in those deadly experimentations which were carried on human subjects in Germany. After the World War II, Nuremberg trials were held (1945-1946) and that lead to the evolvement of Nuremberg code or principles. The principles signify that the humans should not be involved in any scientific experiments without prior permission or informed consent. The violation of human dignity and self respect created extensive moral outrage.[4] This was followed by the Universal Declaration of Human Rights in 1948. The declaration stipulates that all human beings must be treated equally and should be free to exercise their rights.[5]

These incidents have major contribution in the evolvement of Biomedical ethics. After the human experimentations of World War II, other inhuman activities were carried on in which humans were merely used as guinea pigs. The UNIT 731 study was done in China in which the humans were vivisected and infected with lethal infections to see and observe the effects of the infected germs on the human body. Similar behavior was witnessed in the Tuskegee syphilis study in which the Afro-Americans were enrolled in the study. In the experimental studies the victims believed that the doctors were treating them but they had no idea that the doctors were not giving them medications. The cruelty and brutality lead to dehumanization and deaths of vulnerable and helpless individuals.[6] In the year 1966, a physician Henry K Beecher published an article which disclosed the misuse of humans by the American physicians. This article played an important role in widely spreading the news of mistreatment of human subjects.[7] Bioethics then evolved as a result of unethical practices. We can say that Bioethics is a systemic study of moral conduct. The subject established the awareness that ethical standards should be followed while handling humans and informed consent is an important element. All the humans which are part of any experimentation or treatment should know what is going to be done to their bodies and how they are going to be used. The queries which are arising in the new era are also the part of this subject. Questions about what life and death are, how and when a person can be declared as dead, the issues related to abortions and contraception etc have become the part of Bioethics. Other than the discussed topics, other wide range social matters like women rights, occupational health, population control, issues of third world countries are also discussed. Issues related to transplantation, genetic engineering, reproductive techniques and cloning are also dealt in the field of contemporary Bioethics.[8] The changes which are occurring in the modern era have to be discussed and solved. The medical professionals should be informed about the problems and issues which are emerging. That is the reason why Bioethics should be discussed with the upcoming future doctors right from the very beginning of their medical career. According to Hippocrates, "the physician must also add the love of humanity."[9] The doctors are required to act morally other than to be professionally skilled in their field. These days Bioethics is considered to be one of the important components of medical education worldwide. U.SA. was the pioneer in introducing the subject to the medical students. By the year 1994, Bioethics was part of medical curriculum in all the medical colleges of America.[10] Musick in his article mentioned that ethics is an essential subject which needs to be taught to the medical students.[11] That is the reason why Bioethics should be included in the curriculum both at the under and post graduate levels. PMDC stipulates that ethics should be included in the curriculum.[12] In spite of this requirement, there are few

✉ **Dr. Quratul Ain Omaeer**
Senior Lecturer
Department of Anatomy
Bahria University Medical &Dental College
Karachi
Email: docannie2010@gmail.com
Received: 15-10-2016
Revised: 07-11/2016
Accepted: 29-11-2016

colleges of Pakistan which have inculcated Bioethics in the curriculum.[13] A study conducted in Karachi showed that Bioethics taught during the teaching period of medical schools is unsatisfactory.[11]In Pakistan, Aga Khan University was the very first institute to include the subject of Bioethics informally in the curriculum in 1980's.[14] In 2004, Centre of Biomedical Ethics and Culture (CBEC) was established. The centre started a Post graduate Diploma course in Bioethics from 2006 onwards. In 2010, Masters Program was also started there. The alumni of CBEC had later contributed in spreading the knowledge which they had gained.[15] They had established ethical review committee (ERC) in their institutes as well as undergraduate and post graduate training.[16] At Bahria University Medical and Dental College, Ethical Review Committee was established in 2010 and Biomedical ethics was introduced to the medical students in 2015.

Bioethics subject should be incorporated in the medical curriculum as it is a need of the day. This incorporation should be done through horizontal as well as vertical integration so that the subject gets proper importance and integration.[17] The purpose of teaching Bioethics is to stimulate the young minds to the changing times and to introduce them with the new issues which are arising. After getting training in the Bioethics, the medical students would be able to identify the ethical issues and can come up with moral reasoning of the given scenario. Motivation and inspiration are essential factors for Bioethics teaching and imparting training to prepare ethical health professionals. A well constructed Bioethics curriculum is needed as a key component. One of the goals of teaching should be to make a curriculum that should produce interest and enthusiasm in the students.[18] Students keenness can be generated by adding case scenarios and topic related videos and role plays. The discussion generated by the videos and the case scenarios are very beneficial in understanding the subject. Short groups are ideal so all the students can participate actively. In place of lectures, Problem Based learning strategy can play an ideal role in imparting the knowledge of Bioethics and also to generate discussion among the members. Students after taking training, learn to differentiate between the right and wrong in the given situation.[19]

The advancements in technology will bring more and more queries with the passage of time. The issues need to be addressed. Policies and plans have to be designed in order to make a proper setup to ethically reflect upon such problems. The policies should be updated and improved on regular basis.

The institute of Pakistan Medical and Dental Council should make the subject of Bioethics mandatory in all the medical colleges of the country. This step would help the authorities to realize the importance of teaching the new subject. The doctors after getting degree from the medical college will not only be skilled in their professional tasks, but will also be able to think critically and understand the issues around and can come up with rational reasoning.

CONCLUSION:

To conclude Bioethics, a comparatively new subject in Pakistan is need of the day. If we want our students to be morally and ethically reflective upon the present day issues then it is a must to teach them and introduce them with the subject of Bioethics. This will benefit the patients and fellow colleagues. To attain this goal, we need to have faculty trained in the subject of Bioethics. The administration of the colleges and the universities should take initiative to include the subject in the curriculum and to motivate the staff members to get training in the subject.

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STUDENTS CORNER

Students' Documentary Competition on "Perceptions & Attitudes towards Oral Health" by Department of Community Dentistry

Raima Bashir[1], Kulsoom Fatima Rizvi[2]

The Department of Community Dentistry of BUMDC, continued its tradition of yearly organization of a Constructive students' educational activity and arranged an innovative students' Documentary Competition on the subject of "Perceptions & Attitude towards Oral Health" amongst the students of 2nd year BDS. The event took place on Wednesday 28th September 2016, from 11am- 2pm at the Ibn –e- Sina Auditorium of BUMDC. It was conceived by Dr.Kulsoom Fatima Rizvi (H.O.D) who proposed the concept of a students' activity that was healthy, exciting, and educationally stocked. It encouraged the students' cognitive functioning, enhanced their creativity skills, presentation abilities and also helped them acknowledge the theoretical knowledge with its implication and impact on the society. All this was put together in the form of Short Documentary films of 10-15 minutes durationand presented before the audience that comprised of entire medical and dental faculty and all the years of MBBS and BDS students.

The whole class had been divided into 5 groups to inculcate the significance of team work and promote the concept of group study for better understanding during the making of documentary films. The documentaries were based on the topics such as impact of gutka and paan on the society and the reasons behind the increased consumption of this poison among our younger generation. Impact of junk food consumption on the oral and general health was also highlighted. The documentary on mercury hazards (Poison in the Mouth) tried to draw attention of the audience towards the myths and realities regarding the use of amalgam as a restorative material and also tried to answer queries by sharing facts, researches and professional experiences of clinicians. Quackery was another topic selected for documentary that provided an insight of the root cause of this malpractice in the society. All the documentaries were supervised by Dr. Raima Bashir.

✉ **Dr. Raima Bashir**
Senior Lecturer
Department of Community Dentistry
Bahria University Medical and Dental College
Karachi
Email: raimabashir@gmail.com
✉ **Dr. Kulsoom Fatima Rizvi**
Head of Department
Department of Community Dentistry
Bahria University Medical and Dental College
Karachi
Received: 08-11-2016
Revised: 25-11-2016
Accepted: 11-12-2016

The Director General of BUMDC Vice Admiral (Rtd) TahseenUllah Khan and Dean & Principal Health Sciences, Brig (Rtd) Prof. Dr Shaheen Moin were invited as chief guests. Respectable heads and faculty of entire medical & dental sections of BUMDC and the undergraduate students of MBBS and BDS were also invited to provide support and encouragement to the participants. The Jury comprised of Dr Ashar Afaq (HOD Community Dentistry &Vice Principal Dow dental college) and Dr. Shama Asghar (HOD Operative Dentistry, BUMDC) who judged each documentary film on their concept, knowledge delivery via content, and presentations skills and scored them accordingly. The results were compiled by commutating the marks allotted by each jury member.

The competition commenced with a welcome address to all the guests by Dr. Raima Bashir and Dr. Nazish Fatima, the hosts of the event. After recitation of the Quran the event proceeded with an introductory presentation on departmental achievements and a featured video on outcomes and accomplishments of a "Community Support Program" running successfully in BUMDC under the dynamic supervision of Dr. Kulsoom Fatima. Dr. Kulsoom Fatima welcomed the respectable guest, faculty and students of all MBBS & BDS batches and congratulated all the participants and the organizers on the accomplishment of a successful event.

Two guest lectures were also arranged in between the documentaries. First guest lecture was delivered by Dr. Zainab Zadeh in which she highlighted the relationship between oral and psychological health. She emphasized that oral health cannot be attained if one is not psychologically healthy. Her captivating personality and exuberant style really impressed everybody and she was praised with loud applauds. The 2nd guest lecture was on the topic of "Bioethics in Dentistry" and it was delivered by Prof. Dr. Ambreen Usmani. The topic provided informative knowledge on the ethical considerations and its implications and significance with respect to dentistry. This was followed by the last documentary of the program. During the compilation of result the Chief Guest of the event, our honorable Director General of BUMDC was requested to come on stage and express his views on the event. He congratulated the participants and the department with words of tremendous appreciation for working whole heartedly as a team in completion of the event and emphasized that such activities should be conducted on regular basis. He further stated that he was pleased to see excellent documentary films prepared by the students. The ceremony was concluded with prize distribution of

shields and certificates to meritorious students. 1st prize was awarded to documentary film titled "Impact of gutka on oral health" prepared by team M. Zaman, Palwasha khattak, Sarah Jamil, Affaf Naeem, Kashaf Fatima, Paras, Perhe, Bakhtawar, Hassan Riaz and Rizwan Khan and 2nd prize was bagged by film "Quackery: Blessing or Curse" by team Hania Chocksey, Hamna khalid, Sidra Solangi, Moneeba, Syeda Zahra Hassan and Bisma Anis. Honorary shields were also presented to our respected guest speakers and judges. Certificate of appreciation were awarded to the organizers namely Dr. Kulsoom Rizvi, Dr. Raima Bashir, Dr. Nazish Zafar and Assistant Qadeer Ahmed for their tireless efforts in making this event a complete success. Finally Dr. Kulsoom thanked everybody for sparing their precious time for the encouragement of the students for their tremendous hard work. BUMDC inspires the execution of healthy extracurricular activities as they set a platform for all the young nurturing students in building up their confidence, and exploring their hidden potential and talents.

Figure: 1

Group photo with Director General, Dean, judges and departmental faculty

Figure: 2

Prize Distribution Ceremony

Figure: 3

Judges Evaluating Each Documentary

CASE REPORT

Removal of Malfunctioning Biliary Plastic Stent Via Percutaneous Transhepatic Cholangiography

Sehrish Mehmood[1], Irfan Amjad Lutfi[2], Kashif Shazlee[3], S M Qamrul Arfin[4]

ABSTRACT:
Obstructive jaundice is one of the most common presentations of pancreatic cancer. Often the patients present when curative surgical resection is not possible due to late diagnosis. In these cases, palliation is the only option available. However in such cases, endoscopic retrograde cholangiopancreatography (ERCP) is not possible because of surrounding extensive inflammation. This study describes percutaneous transhepatic external biliary drain placement in patients with cancer of pancreatic head when surgical removal is not possible.

Keywords: Malignant obstruction, Pancreatic cancer, ERCP, Transhepatic cholangiopancreatography

INTRODUCTION:

Percutaneous biliary intervention is provided as an adjunct to planned surgical resection or as a palliative procedure for inoperable malignant biliary obstruction.[1] The removal of malfunctioning plastic biliary stents percutaneously is very difficult and not well described previously. The following study describes our clinical experience and different interventional techniques in the management of malfunctioning plastic biliary endoprostheses in patients with malignant obstructive biliary disease.

CASE:

Here we describe a case of a 42-year-male patient, known case of carcinoma of pancreas who presented with obstructive jaundice in gastroenterology clinic, with previous history of gastrojejunostomy and endoscopic biliary plastic stent placement in some other tertiary care hospital. He presented with high grade fever, vomiting and upper abdominal pain. He was then attempted for ERCP but failed because of surrounding extensive inflammation. Then percutaneous transhepatic external biliary drain was placed to limit the risk of ascending cholangitis. After 3-4 days, the patient's condition started to deteriorate as the LFTs were deranged and total leucocyte count reached up to 63,000/ mm^3. Because the patient was not fit for surgery, this left us with no option than to proceed with percutaneous intervention. Hence he was again shifted to interventional radiology department and the plastic stent was effectively removed using the polypectomy snare via percutaneous approach and metallic stent was placed successfully as a palliative treatment. Percutaneous transhepatic cholangiopancreatography is usually performed in those clinical settings where endoscopic retrograde cholangiopancreatography is not possible or in the cases of its failure. Patient is now doing well clinically, with normal leucocyte count and liver function tests.

✉ **Dr. Sehrish Mehmood**
Resident
Department of Radiology
Ziauddin University Hospital
Karachi
Email: drsehrish_mahmood@hotmail.com
✉ **Dr. Irfan Amjad Lutfi**.
Interventional Radiologist
Department of Radiology
Ziauddin University Hospital
Karachi
✉ **Dr. Kashif Shazlee**
Head of Department
Department of Radiology
Ziauddin University Hospital
Karachi
✉ **Dr. S M Qamrul Arfin**
Gastroenterologist
Ziauddin University Hospital
Karachi
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Figure: 1

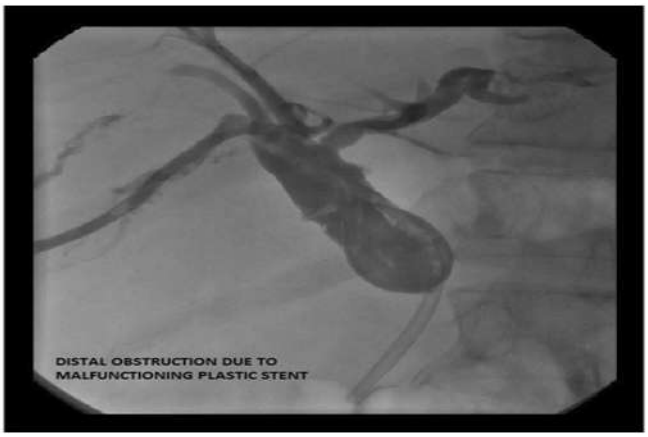


Figure: 2

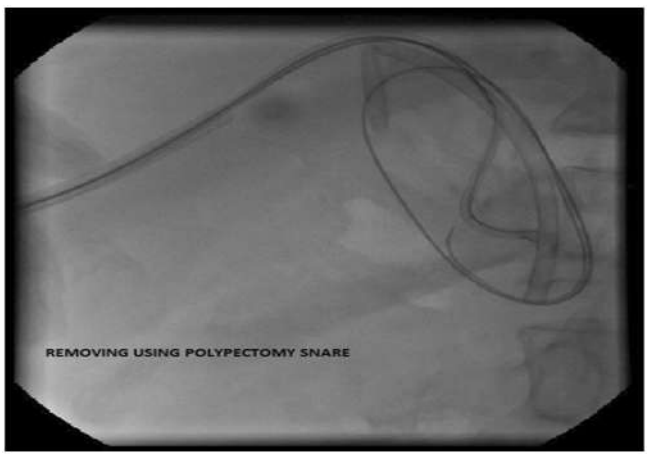


Figure: 3

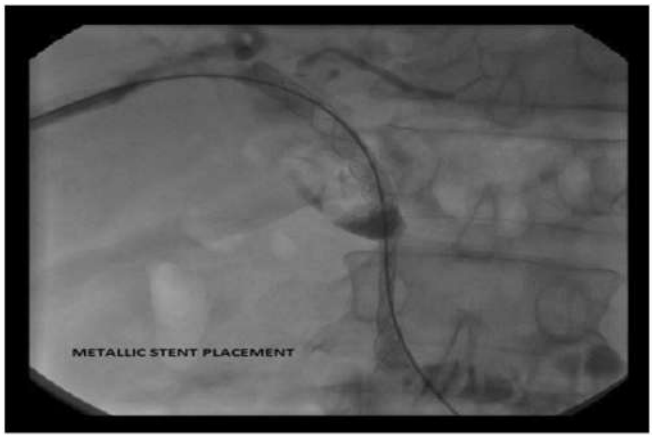
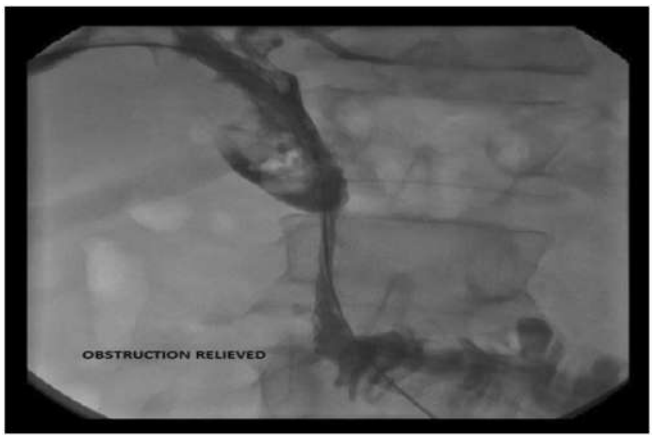


Figure: 4



DISCUSSION:

Malignant jaundice occurs when there is blockage of the biliary tract, either by neoplastic infiltration or external compression. The common neoplasms in majority of the cases are cholangiocarcinoma and adenocarcinoma of the pancreatic head.[2] Endoscopic retrograde cholangiopancreatography (ERCP) is considered as the first-line diagnostic and therapeutic modality in patients with jaundice secondary to malignant biliary obstruction. Palliation of these patients is achieved by insertion of plastic stents during the same session.[3,4] Infection or colonization by bacteria can occlude the stent by forming bacterial clump or sludge formation,[5,6] thus, increasing the risk of cholangitis. Other complications related to the stents include migration, occlusion, and intestinal perforation.[7] Placement of percutaneous transhepatic external biliary drain is considered as the best option. This relieves jaundice and sepsis and decreases the risk of hepato-renal failure. In patients deemed unfit for surgery due to co-morbidity or an unresectable tumor, percutaneous biliary stenting is performed.[1] The percutaneous transhepatic approach may be a life-saving procedure in the management of dysfunctioning plastic endoprostheses. Percutaneous transhepatic removal of the plastic stent can be applied using a goose-neck snare. Replacement of the plastic stent with a metallic stent that can expand to a diameter of 8-10 cm, which is three times greater than that of plastic stents in common use, may be a good option to overcome this problem.[3,8,9,10]

CONCLUSION:

Biliary obstruction due to malignant strictures of bile ducts or irresectable hepatobiliary cancers may be relieved surgically. On the other hand, nonsurgical biliary drainage can be achieved either through percutaneous transhepatic approach or endoscopically. Percutaneous transhepatic biliary drainage (PTBD) is effective and appropriate for both tumor ingrowth and overgrowth. It is an alternative intervention after failed endoscopic management.[1] Many different options exist for management of the dysfunctioning plastic endoprostheses. The interventional radiologist should be familiar with different techniques and know that all these techniques can be performed with high success and very low complication rates.[3]

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LETTER TO EDITOR

Diagnostic Errors in Undergraduate Students: A threat to Clinical Practice

Sara Shakil

To,
The editor,

There has been an alarming increase in the prevalence of medical errors which include misdiagnoses, surgical mistakes and skill deficiencies in undergraduate students.[1] The ultimate goal of undergraduate teaching is to improve patient safety by reducing the likelihood of diagnostic errors in medicine.There are many reasons that underpin this situation.[2] Firstly, cognitive deficiencies in achieving accurate and plausible diagnosis pulls the student back from thinking critically. Secondly, inadequacy in communicating with patients, attendants and other health care professionals plays a key role towards development of diagnostic errors. Effective communication is an essential part of building and maintaining good physician-patient and physician-colleague relationships.[3] These skills help people to understand and learn from each other, develop alternate perspectives, and meet each other's needs. Lack of clinical reasoning skills and inefficiency in thinking scientifically are other factors that contribute to these errors.Besides these causes, there are errors in the healthcare system which contribute to this dilemma. Technical errors include unavailability of latest equipment or carelessness of laboratory staff resulting in dissemination of incorrect test results.[4] Hence several strategies can be adopted to address these issues and improve the current situation in medical colleges.[5] Good training and ongoing professional development programs can develop clinical expertise in medical undergraduates. Communication skills can be learnt through structured small group learning in tutorials and clinical settings to overcome emotional and stress barriers. Cognitive deficiencies can be catered by introducing simulation based medical education right from the beginning of medical curriculum. Simulation may be used extensively ranging from basic practical skills learning in a skills lab to complex communication skills teaching using simulated patients. Lastly, constructive feedback may be provided to the undergraduates since it is the most essential component of student learning. It fosters student's growth, provides direction and helps to boost confidence, increase motivation and self-esteem. These approaches would hopefully make the current situation a little better if not improving it completely.

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Dr. Sara Shakil
Senior Lecturer
Department of Medical Education
Bahria University Medical & Dental College
Karachi
Email: drsarashakil@gmail.com

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The Cardiac Society of Australia and New Zealand. Clinical exercise stress testing. Safety and performance guidelines. Med J Aust 1996; 164: 282-4

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Cancer in South Africa [editorial]. S Afr Med J 1994;84:15

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