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FOR EXCELLENCE IN MEDICAL EDUCATION (AEME)**

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Editorial Correspondence should be addressed to: Editor-in-Chief, AJSMU, Jinnah Sindh Medical University, Rafiqi H.J. Shaheed Road, Karachi 75510; Tel: 99204776; 35223811-15/301, 320

Email: ajsmu@jsmu.edu.pk; Website: www.jsmu.edu.pk/ajsmu; Fax: 99201372

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What Investigators Must Know?

Jamshed Akhtar

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A reader does not have to ponder about the author while reading a novel or story book, however issue is not straightforward in academic writings. The authorship issue remained controversial thus frequently debated in editors' meetings. Many articles written on the subject is testament to its importance¹. Issue of who can be an author and who cannot, often raises conflict between journal editors and investigators. It is unethical to omit the name of a person who has made significant contribution to the research and its write up, while giving credit to those by including names in authorship, who were not involved in research.

- The International Committee of Medical Journal Editors (ICMJE) has proposed following criteria for authorship².
- "Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved."

The ICJME guidelines cover most aspects but are not comprehensive. Some areas are vague and open to interpretation. Other guidelines on the subject are also available in literature³. As opinion about authorship criteria varies, an emphasis has been placed to further debate this issue⁴.

Shared values in scientific research include honesty, accuracy, efficiency and objectivity. These values are equally applicable to authorship thus, only those who

actually participated in research be given credit⁵. It is common to find the name of persons who belonged neither to the specialty nor to the institute where the study conducted. This raises the question as to what might be the reason behind such practices. In Pakistan, one of the criteria for the promotion to the faculty posts is the number of publications against one's credit. With lack of infrastructure for research at many medical universities / medical colleges and hospitals, the incumbent seeks ways out of this perceived hurdle. The easy solution is to get one's name in any article that is send for publication. Medical journal editors have equal responsibility to discourage this trend. They can be vigilant while initially assessing the articles for authorship claim. Gift authorship is a type of publication misconduct⁶. It is proposed to get approval for authorship when research proposal is submitted to the Institutional Review Boards (IRB). The name of all the authors and their potential roles needs approval at this stage. IRB approval letter is an important document to curb down this misconduct.

Number of authors per manuscript is also an issue. Editors remain skeptical when they find large number of authors for case reports, viewpoints, letters, case series etc. Editors cannot dictate authors as to such practices but can ask for explanation as to what might be the contribution of each author to the manuscript in above-mentioned categories. Number of authors can be many in multicenter, multidisciplinary studies like randomized controlled trials. It also depends upon the scope of the study. Editors' role is not the policing in addressing authorship issues. It is their responsibility to encourage fair practices. To address some of these issues, journals have incorporated headings of contributorship and acknowledgment. The services of research officers for data collection, statisticians for data analysis and epidemiologists for suggesting study design may fall under these headings until they played significant role in conceiving the idea and got involved in all aspects of manuscript writing and being responsible and accountable for integrity of the results.

Correspondence: Prof. Jamshed Akhtar, Department of Paediatric Surgery, National Institute of Child Health, Jinnah Sindh Medical University, Karachi, Pakistan.

E mail: jamjim88@yahoo.com

Acknowledgement is another important area to be addressed. It is observed that institutional / department heads and many other irrelevant persons are acknowledged for no particular research related activity. Editors frequently receive request to change the order of authorship after initial submission. Editors usually do not entertain such a request especially if it is not from all the authors and without a convincing reason. COPE guidelines can be referred to in this context⁷.

A large number of issues in relation to authorship highlight importance of educating researchers. Pakistan Association of Medical Editors (PAME) has been conducting workshops of the subject of publication ethics and medical writing. Resource material is present on PAME website⁸. The editorial board of AJSMU also offers its services in facilitating such educational activities in order to ensure ethical conduct and reporting of research.

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Authorship

An “author” is generally considered to be someone who has made substantive intellectual contributions to a published study, and biomedical authorship continues to have important academic, social, and financial implications. Some journals now request and publish information about the contributions of each person named as having participated in a submitted study, at least for original research. Editors are strongly encouraged to develop and implement a contributorship policy, as well as a policy on identifying who is responsible for the integrity of the work as a whole.

(Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication)

Comparison of Serum Levels of Vitamin D with Asthma Severity in Children in a Tertiary Care Hospital of Karachi

Afshan Mehboob Khan¹, Khalid Mehmood Ahmed Khan², Khatidja Pardhan²
and Abdul Shakoor Memon¹

ABSTRACT

Objective: The purpose of this study is to measure the serum vitamin D level in asthmatic children and to compare this level with severity of asthma.

Methods: A total number of 44 subjects (aged between 6-14 years) of both gender were included in this study. The study was carried out from October 2014 to April 2015. Subjects were diagnosed asthmatic patients according to GINA guideline. A written and verbal consent was taken from the subject's guardians after explaining about the study. Subject's physical parameters included age, sex, body mass index, forced vital capacity (FVC), forced expiratory volume in 1st sec (FEV1) and FEV1/FVC ratio. Serum 25(OH)D was tested by Vitamin D ELISA kit and pulmonary function test (spirometry) by spirometer. Statistical analysis was conducted using SPSS software version 19.

Results: A total number of 44 asthmatic children (26 boys and 18 girls) were recruited for the study. Mean age of subjects was 10.06±2.23 years. Median BMI was 10th percentile. Mild persistent asthmatics were 11 while moderate persistent asthmatic children were 33. Out of 44, 36 (81.81%) cases had insufficient and 8 (18.2%) had deficient levels of vitamin D. The comparison of insufficient and deficient levels of serum vitamin D with severity of asthma showed that 11 (100%) mild persistent asthmatic children had insufficient level of vitamin D. No case of deficient level of vitamin D was found in this asthmatic group. 25 (75.75%) moderate persistent asthmatic children had insufficient levels of vitamin D and 8 (24.24%) children had deficient levels in this group. We did the comparison of pulmonary function test in asthmatics with insufficient and deficient vitamin D levels. We found significantly low FEV1 (0.85L) in asthmatics with deficient vitamin D level than asthmatics with insufficient vitamin D level (1.20L) (p<0.05).

Conclusion: In our study, it was revealed that hypovitaminosis D is much more prevalent in asthmatic children. Comparison between different categories of asthma showed that serum vitamin D level was decreased with severity of asthma.

Key words: Asthma, Vitamin D, asthmatic children, spirometry.

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عنوان: وٹامن D کے مختلف مقدار کے سیرم (Serum) کا ایک تیسرے اعلیٰ درجہ (Tertiary) کے ہسپتال کے بچوں میں وٹامن D کی شدت تقابلی کا جائزہ۔
دمہ ایک دائمی سوزشی مرض ہے جو سانس کی نالی کو پتلا کر دیتا ہے جس کی وجہ سے سانس لینے میں کھراہٹ اور کھانسی پیدا ہو جاتی ہے۔ اور اس کا سانس لینے میں رکاوٹ سے تعلق ہوتا ہے۔ سانس دانوں نے وٹامن ڈی کی کمی کو دمہ کے مرض سے جوڑا ہے۔ دمہ اور دوسری حساس بدظمی بیماریوں کا بھلاؤ تقریباً سارے ملکوں میں بڑھ رہا ہے۔
مقصد: اس تحقیق کا مقصد دمہ سے متاثر بچوں میں وٹامن ڈی کے سیرم کی مقدار معلوم کرنا اور اس مقدار کو دمہ کی شدت سے تقابلہ جائزہ کرنا ہے۔
طریقہ: چھ الیس دو نوں جنسوں کے بچے جن کی عمریں ۶ سے ۱۶ سال تک تھیں اس تحقیق میں شامل کیا گیا۔ مطالعہ اکتوبر ۲۰۱۴ء سے اپریل ۲۰۱۵ء کے درمیان کیا گیا۔ بچوں کو GINA رہنما اصول کے تحت دمہ کی تشخیص کی گئی تھی۔ بچوں کے وٹامن ڈی کی تحقیق کے مطالعہ کی معلومات سمجھائی گئیں اور ان سے تحریری راضی نامہ لیا گیا۔ مطالعہ بچوں کی عمر، جنس، قد اور وزن کی معلومات کی گئی۔ اسکے ساتھ forced expirator volume in 1st sec (FEV1) اور viral capacity (FVC) کو ناپا گیا۔ سیرم 25(OH)D کی مقدار ELISA kit کے ذریعے اور سینے کے نفل Spirometer کے ذریعے سے معلوم کیا گیا۔
نتیجہ: اس تحقیق سے یہ ثابت ہوا ہے کہ وٹامن ڈی کی کمی دمہ والے بچوں میں زیادہ پائی جاتی ہے۔ جیسے جیسے وٹامن ڈی کی مقدار کم ہوتی ہے دمہ کی شدت میں اضافہ ہوتا جاتا ہے۔

1 Department of Physiology, Sir Syed College of Medical Sciences for Girls, Karachi, Pakistan.

2 Department of Paediatric, National Institute of Child Health, Karachi, Pakistan.

Correspondence: Dr. Afshan Mehboob Khan, Department of Physiology, Sir Syed College of Medical Sciences for Girls, Karachi, Pakistan.

Email: drafshanzafar@gmail.com

INTRODUCTION

Asthma is a chronic inflammatory disease that causes narrow airways resulting in wheezing, breathlessness, and coughing with variable airflow obstruction³. Deficiency of Vitamin D was seen in children with asthma and other allergic disorders. Deficiency of Vitamin D was a strong correlate for asthma, allergic rhinitis and wheezing¹.

The prevalence of allergic diseases and asthma has been increasing in western and industrialized countries. In western countries vitamin D deficiency has occurred even provided in the supplements and in the sufficient sun light regions of the world¹².

In Pakistan, vitamin D deficiency was much more prevalent in our community in all age groups and in either gender¹⁴.

Airway epithelial cells contain enzymes that convert circulating 25-OH-vitamin D₃ to its active form, 1,25-(OH)₂-vitamin D₃. This active form of vitamin D has effects in response to infections and may decrease the inflammation that is the result of these infections⁹. Vitamin D metabolism effects the functions of epithelial cells, T-cell B-cell, and dendritic cells⁸. The important role of vitamin D is mainly by antimicrobial peptide for example cathelicidin⁵.

The aim of this study is to estimate serum vitamin D levels in asthmatic children and to compare these levels with severity of asthma.

METHODOLOGY

Study design and duration

This case control study was conducted during October 2014 to April 2015 in the Department of Physiology, Basic Medical Sciences Institute (BMSI), Jinnah Postgraduate Medical Centre (JPMC) Karachi, in collaboration with National Institute of Child Health (NICH) Karachi, under kind supervision of Dr. Abdul Shakoor Memon, Department of Physiology. Approval was taken from Institutional Ethical Review Board (IERB) of NICH, Karachi, for conducting the research (IERB No: 09/2014).

Selection of subjects

A total number of 44 diagnosed asthmatic children of both gender (aged 6-14 years) from NICH were included in this study. The asthmatic children were diagnosed and classified according to Global Initiative for Asthma Guideline⁴. Participants who have history of consumption of any supplement of vitamin D or drugs that modulate serum vitamin D levels were excluded from the study also patients who have chronic pulmonary disease e.g. cystic fibrosis, Bronchiectasis were not included in this study.

Grouping of subjects

1. According to asthma severity (mild persistent asthma, moderate persistent asthma).
2. According to serum vitamin D levels (asthmatics with insufficient level, asthmatics with deficient level).

Determination of BMI

Stadiometer was used to measure the weight of all subjects in kilograms (Kgs) and Height in centimeter (cms). The height in cm was converted to meters (m). BMI is calculated by Quetelets index. $BMI = \text{weight in kg} / \text{height in m}^2$

BMI was defined according to WHO percentile references according to age (2007).

Spirometry

Spirometry was done by vitalograph compact spirometer model 6600, Ennis company, Ireland. It was done according to user manual.

Determination of Serum Vitamin D

Serum vitamin D level was determined by 25-Hydroxyvitamin D kit, cat no. 1971, cobas (Holick, 2009).

Categorization of vitamin D (ng/ml)

sufficient >30
insufficient between 10-30
deficient < 10

The asthmatic children were diagnosed and classified according to Global Initiative for Asthma Guideline (GINA guideline, 2008 and 2015).

Mild persistent

Symptoms more than once a week but less than once a day
Exacerbations may affect activity and sleep
Nocturnal symptoms more than twice a month
FEV₁ or PEF 80% predicted
PEF or FEV₁ variability 20–30%

Moderate persistent

Symptoms daily
Exacerbations may affect activity and sleep
Nocturnal symptoms more than once a week
Daily use of inhaled short-acting b₂-agonist
FEV₁ or PEF 60–80% predicted
PEF or FEV₁ variability 30%

Statistical Analysis

Data was entered in excel and was converted in SPSS version 19 for further analysis. Descriptive analysis was done for all continuous and categorical variables. Mean and standard deviation were calculated for all continuous variables like age and BMI. Frequency and percentages were calculated for all categorical variables like gender, vitamin D. Chi square test for categorical

variables. T test for continuous variables. At 95% confidence interval $p < 0.05$ was used to assess the statistical significance.

RESULTS

Table 1 describes the data of asthmatic children. A total number of 44 asthmatic children (26 boys and 18 girls) were recruited for the study. Mean age of subjects was 10.06 ± 2.23 years. Median BMI was 10th percentile. Mild persistent asthmatics were 11 while moderate persistent asthmatic children were 33.

Table 1: Demographic data of subject

Number of subjects		44
Age (years)		10.06±2.23(SD)
Gender	Girls	18(40.9%)
	Boys	26(59.1%)
BMI percentile		10(1.5-25)
Severity of asthma	Mild persistent	11
	Moderate persistent	33

Table 2 shows the categorization of serum vitamin D into insufficient and deficient levels and the number of patients related to these two categories of vitamin D. Out of 44, 36(81.81%) cases had insufficient and 8(18.2%) had deficient levels of vitamin D.

Table 2: Comparison of insufficient and deficient levels of serum Vitamin D in asthmatic children

Variable	Case n =44
Vitamin D Insufficient level(10-29ng/ml)	36 (81.8%)
Vitamin D deficient level (< 10ng/ml)	8 (18.2%)

Table 3 shows the comparison of insufficient and deficient levels of serum vitamin D with severity of asthma. 11 (100%) mild persistent asthmatic children had insufficient level of vitamin D. No case of deficient level of vitamin D was found in this asthmatic group. 25 (75.75%) moderate persistent asthmatic children had insufficient levels of vitamin D and 8 (24.24%) children had deficient levels in this group.

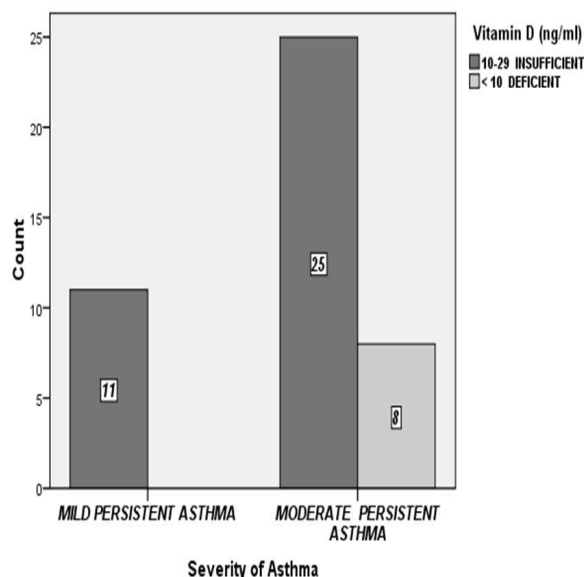
Table 3: Comparison of insufficient and deficient levels of serum Vitamin D and severity of asthma

Variables	Mild persistent asthma n =11	Moderate persistent asthma n =33
Vitamin D insufficient level	11 (100%)	25 (75.75%)
Vitamin D deficient level	0	8 (24.24%)

In table 4, we did the comparison of pulmonary function test in asthmatics with insufficient and deficient vitamin D levels. We found significantly low FEV1 (0.85L) in asthmatics with deficient vitamin D level than asthmatics with insufficient vitamin D level (1.20L) ($p < 0.05$).

Table 4: The comparison of pulmonary function test between asthmatic children with insufficient and deficient serum Vitamin D levels

Variables	Asthmatic with insufficient vitamin D Mean±SD	Asthmatic with Deficient vitamin D Mean±SD	p-value
FVC(L)	1.44±0.08	1.31±0.37	0.584
FEV(L)	1.20±0.07	0.85±0.03	0.036**
FEV1/FVC%	84.62±11.36	82.68±17.65	0.696



DISCUSSION

In this study, we compared the serum levels of vitamin D with asthma severity in children in a tertiary care hospital of Karachi. Previous study by Masood et al,¹⁴ showed that vitamin D deficiency was much more prevalent in our community in all age groups and in either gender.

In our study, 36(81.8%) children had insufficient levels while 8 (18.2%) had deficient levels of vitamin D. Our results are in agreement with the similar studies by Uysalol M et al,¹⁹ and Chinellato et al.²

Asthma is characterized by airway inflammation with enhanced activity of Th2-cells, which then cause IgE production, resulting in Eosinophilic airway inflammation and hyperresponsiveness^{10,17}.

Vitamin D enhances the production of IL-10 as an anti-inflammatory cytokine by human T and B cells⁶. Therefore, fluctuations in vitamin D levels may be correlated to the inflammatory state of the disease¹⁶.

In this study, the comparison of pulmonary function test between asthmatics with insufficient and deficient levels of vitamin D was done which showed significantly low FEV1 in asthmatics with deficient vitamin D levels than the asthmatics with insufficient vitamin D levels. We did not find any significant difference of FVC in both groups. Similar results were shown by Somashekar AR,¹⁸ who had low FEV1 in their asthmatic children with deficient vitamin D levels but he noticed significant differences of FEV1/FVC% in both groups which was not observed in our study.

Black and Scragg¹⁵ found that serum vitamin D levels were positively associated with FEV1 and FVC in United States population. However, Maalmi et al.,¹³ reported that serum vitamin D levels were slightly associated with FVC but no association was found with FEV1 and FEV1/FVC%.

Litonjua et al.,¹¹ put forward that low vitamin D levels were associated with worse bronchial asthma symptoms, more use of medication and poorer lung functions measures.

CONCLUSION

In conclusion, Vitamin D was significantly lower in asthmatic children. A direct and significant relationship was found between vitamin D and pulmonary function test outcomes in asthmatic children. Measuring serum vitamin D levels should be considered as a routine assessment of children with bronchial asthma. It is recommended that improving vitamin D status may help in the primary prevention of asthma and its exacerbation. Clinical trials of vitamin D supplementation are recommended to prevent asthma exacerbation.

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Stress and the Onset of Type 2 Diabetes

Mehwish Nisar¹, Muhammad Waqas Nisar Ahmed², Beenish Nisar Ahmed³,
Arshi Imran⁴ and Sana Nisar Ahmed⁵

ABSTRACT

Introduction: The positive response of a correlation between psychological stress and impaired diabetes control is very old. Thomas Willis commented on the ability of "nervous liquors" to affect diabetes in the 17th Century, and William Osler in the 19th Century. Now it is well accepted that psychological reaction to stressors, leads to various endocrine abnormalities that antagonize the action of insulin. But, until recently, there has been very little research evidences are available to confirm that there is a connection between high stress state and the onset of diabetes. In this study we are trying to evaluate the basic association, of the presence of high level of stress before the onset of type 2 diabetes.

Materials & Methods: A retrospective cross-sectional study was conducted on 339 patients with Type II Diabetes, within one year of onset of the disease, presenting at National Institute of Diabetes and Endocrinology, Dow University of Health Sciences, Karachi between December 1, 2015 to May 31, 2016. Data was collected using a validated questionnaire, Holmes Rahe Life Stress inventory containing 51 stressful events. All the data was sorted and analyzed on Statistical Package Social Sciences (SPSS) Version 22.

Results: Out of 339 patients, 68.73% (n=233) individuals reported with high levels of stress. Males (61.8%, n=144/233) were found to be more frequently associated to high stress levels as compared to females (38.2%, n=89/233). Majority of the individuals belonged to the age group 40-49 years (51.5%, n=120/233), while a significant fraction had family history of diabetes (n=188/233, 80.6%).

Conclusion: This study reported that a significant number of our patients were in a state of high stress before they had diabetes. This shows a positive correlation between the onset of diabetes and the level of stress. It can be concluded that stress management will play a very important role in decreasing the incidence of diabetes. Because of stress management, people can also delay the onset of diabetes, which is present in their genes.

Key words: Onset of type 2 diabetes, stress.

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عنوان: ذہنی دباؤ اور ذیابیطس کی بیماری کا آغاز

مقصد: کسی انسان کا مستقل ذہنی دباؤ میں رہنا اور اسکے خون میں شوگر کی مقدار کا قابو میں نہ رہنا، یہ ایک ایسا تعلق ہے جو زمانہ قدیم سے زیر بحث ہے۔ سترویں صدی کے آغاز میں ولیم اوسلر اور تھامس ویلیس نے یہ خدشہ ظاہر کر دیا تھا کہ ذہنی دباؤ، ذیابیطس کا پیش خیمہ بن جاتا ہے۔ اب یہ بات مکمل طور پر تسلیم کی جا چکی ہے کہ ذہنی دباؤ کی وجہ سے جسم میں جو تبدیلیاں آتی ہیں، ان کی وجہ سے جسم میں ایسے ہارمون پیدا ہوتے ہیں جو انسولین کو کام کرنے سے روکتے ہیں اور انسان کو ذیابیطس کی مریض بنا دیتے ہیں۔

مقصد: اس تحقیقی مطالعہ میں ہم نے ذہنی دباؤ اور ذیابیطس کے آغاز میں تعلق معلوم کرنے کی کوشش کی ہے۔

طریقہ: اس تحقیق میں ۳۳۹ مریضوں کو شامل کیا گیا ہے۔ یہ وہ مریض تھے جن کو ذیابیطس کا مرض ایک سال کے عرصے میں ہوا تھا۔ ان سب سے ہوٹس راہی سے منسلک سوالنامہ بھرا گیا اور پھر تمام سوالات کے پوائنٹس کو ملا کر اسکور بنایا گیا۔

نتیجہ: ۳۳۹ مریضوں میں سے ۲۳۳ مریضوں میں ذہنی دباؤ کی شدت بہت زیادہ تھی یعنی ۶۹ فیصد مریض ذیابیطس کے آغاز سے ایک سال قبل شدید قسم کے ذہنی دباؤ اور پریشانیوں میں گھرے ہوئے ہوتے ہیں۔ ایک اور اہم مشاہدہ یہ ہوا کہ ان کے خاندان میں ذیابیطس کا مرض پہلے سے موجود تھا۔ اس سے اس بات کو تقویت ملتی ہے کہ لمبے عرصے تک ذہنی دباؤ میں رہنے سے ذیابیطس کا خطرہ بڑھ جاتا ہے۔ حاصل مطالعہ: اگر ذہنی دباؤ میں مبتلا افراد اپنے ذہنی تناؤ کو مناسب طریقے سے کم کریں اور ضرورت پڑنے پر علاج بھی کرائیں تو ذیابیطس جیسے مرض میں مبتلا ہونے کا خطرہ ٹل سکتا ہے۔

1 Sr. Lecturer, General Practitioner, Dow University of Health Sciences, Karachi, Pakistan.

2 Lecturer, Member of Medical Examination Committee, Jinnah Sindh Medical University, Karachi, Pakistan.

3 ENT Consultant, Shifa International Hospital, Islamabad, Pakistan.

4 Medical Officer, Atique Orthopedic & Medical Center, Karachi, Pakistan.

5 Incharge, Special Children's Education Institute, Karachi, Pakistan.

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Correspondence: Dr. Muhammad Waqas Nisar Ahmed, Lecturer, Member of Medical Examination Committee, Jinnah Sindh Medical University, Karachi, Pakistan.

Email: drwaqasnisar@yahoo.com

INTRODUCTION

Stressful experiences have been associated to the onset of diabetes in individuals already predisposed developing the disease. An English physician in early 17th century convicted “prolonged sorrow” for the onset of diabetes¹.

Several studies have been conducted to identify stress as a factor triggering onset of diabetes^{2,3}. Kawakami et al suggested stressful working conditions to account for increased risk of developing type 2 diabetes mellitus³.

Mooy et al reported an association between chronic stress and type 2 diabetes in a study based on general population. This study included individuals initially non-diagnosed with diabetes to exclude the chances that the disease itself resulted in stress⁴.

Stress refers to a state of an individual who has shown non-compliance with emotional trauma whether real or conceived as a mere notion. Depression is a major predisposition to diabetes; however, it is being brought into current focus that day-to-day stresses, constant “low” moods, and a general state of non-contentment inadvertently lead to the onset of the disease⁵.

This is largely supported by the diabetes statistics given by the US Department of Health and Human Services for 2010, stating 26.9% of all people aged 65 or older to be diabetic, as compared to 11.3% persons in age group 25 or older, rendering to the depressed state of many a people in the geriatric age group⁶.

Bjorntorp⁷ in his study elucidate this linkage of stress and onset of diabetes according to which, the psychological reaction to the stressful agents triggers hypothalamo-pituitary-adrenal (HPA) axis. This reaction sequentially amends the normal endocrine productions leading to high cortisol and low sex hormone levels, all of which antagonizes insulin response.

Stress precipitating in diabetes is in contradiction to the concept of homeostasis as stated by McEwen et al⁸, but in accordance with the physical laws of stress, strain and load. The body adapts to the changes and evolves and responds by changes in its normal physiologic mechanisms that ultimately jeopardize the body’s own well being.

The discovery of stress as a causative factor of diabetes II serves to prove beneficial in the management of this severely debilitating metabolic syndrome. It opens therapeutic expanses in managing and more importantly, preventing, the syndrome by controlling stress levels in people who are prone to developing the disease, especially in patients with a strong family history of the diabetes.

METHODS

Study setting and Participants:

This was an observational cross-sectional study conducted at the National Institute of Diabetes and Endocrinology (NIDE), Karachi over a period of 6 months from December 1, 2015 to May 31, 2016. The study population included 339 patients with Type 2 Diabetes Mellitus presenting at NIDE. The study included only patients who were diagnosed with Type 2 DM within the past one year.

Collection of Data:

Data was collected using a self-administered questionnaire, Holmes and Rahe Stress Scale. Formal Consent was also obtained from all participants. The Holmes and Rahe Stress Scale, also known as Social Readjustment Rating Scale (SRSS) is a validated questionnaire widely used to measure the levels of stress in an individual and to determine whether stress contributes to the development of a certain illness. It comprises of 51 stressful events, where each event has been assigned Life Changing Units (LCU). These LCUs are multiplied by the time experienced in the last year. Total of all the 51 questions is added to get the final score. The individuals with total score of 150 or less are considered to be at low stress levels. Those with score from 151 to 300 are at moderate levels of stress, while individuals with scores more than 300 are at high levels of stress.

Analysis of Data:

A sample size of 339 was calculated with 95% confidence interval, with odd ratio 3:12 and 5% estimated error. This sample size was calculated by using software open epi

The data was entered and analyzed on SPSS version 22. Frequency and percentages were calculated for qualitative variables whereas means, standard deviations were calculated for quantitative variables. P-values were calculated to determine the significance of the data using Pearson Chi Square Test.

RESULTS

A total of 339 diabetic patients were found in accordance with the inclusion criteria during the study period.

The basic significant finding of our study is that majority of the patients (n=233/339, 68.73%) were suffering from high levels of stress, before the onset of diabetes. About 20.64% (n=70/339) individuals were found with moderate level of stress, while low stress levels were present in 10.62% (n=36/339) individuals.

Table 1: Stress in diabetic patients in relation to demographic variables

	Low Stress	Moderate Stress	High Stress	Total	P-Values
Frequency:	36 (10.6%)	70 (20.6%)	233 (68.7%)	339	
Male/Female:	18/18	27/43	144/89	189/150	<0.002*
Age groups:					
29-39 years	7	3	51	61	<0.000*
40-49 years	8	57	120	185	
50-59 years	5	8	61	74	
60-64 years	16	2	1	19	
Family Diabetic History (Yes/No)	35/1	68/2	188/45	291/48	<0.000*
Age of Onset					
1-3 months	21	38	96	155	<0.007*
4-6 months	10	11	92	113	
7-9 months	5	18	41	64	
10-12 months	0	3	4	07	

*p < .05

If we explain the details of outcome then, out of the 339 diabetic patients, majority were males (n=189/339, 55.75%) while 44.25% were females (n=150/339). While out of the 233 patients reporting high level stress, 61.8% were males (n=144/233) while 38.2% were females (n=89/233) [Table: 1].

The age of the 339 participants ranged from 29 years to 64 years, giving the mean age of 45.69±6.973 years. Out of the total 339 participants, majority belonged to age group 40-49 years (n=185/339, 54.5%). While out of the 233 participants diagnosed with High Stress Level, majority belonged to age group 40-49 years as well (n=120/233, 51.5%) [Table: 1].

Out of the 339 individuals that participated in our study, family history of diabetes was reported in 85.84% (n=291/339) individuals. Out of these 291 individuals, high level stress was reported in majority of individuals (n=188/291, 64.6%) [Table: 1].

Our study included only those individuals who were diagnosed with diabetes within the past 1 year. However, for our study population that included 339 participants, this duration ranged from 1 month to 11 month with a mean of 4.26±2.761 months.

Majority of the individuals were in the first three months of their diagnosis of diabetes (n=155/339, 45.7%). Moreover, out of the 233 individuals that reported with High Stress Levels, majority were in the first three months of their diabetes duration (n=96/233, 41.2%) [Table: 1].

Out of the 339 individuals that participated in the study, majority were housewives (n=104/339, 30.6%), followed by government employees (n=60/339, 17.7%).

Table 2: Stress levels in diabetic patients in relation to occupation.

Occupation	Diagnosis			Total	P-Values
	Low Stress	Moderate Stress	High Stress		
Advocate	0	0	1	1	<0.000*
Businessman	0	0	6	6	
Clerk	0	0	4	4	
Cook	0	0	1	1	
Director	0	1	2	3	
Doctor	0	0	19	19	
Driver	0	3	18	21	
Engineer	0	15	2	17	
Government employee	1	2	57	60	
Housewife	11	42	51	104	
Jobless	0	0	24	24	
Nursing	7	0	0	7	
Pastor	0	0	1	1	
Peon	1	0	0	1	
Private Job	0	2	18	20	
Professor	0	4	0	4	
Retired	16	1	7	24	
Teacher	0	0	22	22	
Total	36	70	233	339	

*p < .05

However, out of the 104 housewives, 51 reported with high-stress level (n=51/104, 49%), while out of the 60 government employees, 57(95%) reported with high-stress levels. Thus, the government employees were most frequently associated with high stress levels in relation to house wives [Table: 2].

DISCUSSION

Our study suggested that majority of the diabetic individuals were suffering from high-level stress and majority were in the first 3 months from onset of diabetes. Thus, our study has provided a remarkable relation between stress and onset on diabetes, and we can determine stress as a strong causative factor of type-2 diabetes.

Stress causes the release of glucocorticoids which induce an inflammatory response and increase lipid and glucose mobilization in the body (the “fight or flight response”), depress the powerful anabolic insulin pathway and give way to the release of the catabolic epinephrine pathway. Chronic stress thus leads to an increasing insulin resistance- favoring the development of diabetes type II. Hyperlipidemia caused by the release of steroid hormones in response to stress is one of many factors contributing to development of peripheral insulin resistance.

The body's response to stress- by suppression of the fuel conserving insulin pathway and activation of the epinephrine response and hyperlipidemia- is a mechanism evolved to fight acute emergency states of the body. However, a chronic such condition will be followed by insulin resistance- a predisposing factor of the metabolic syndrome diabetes type II.

When insulin binds to its receptor, the receptor auto-phosphorylates and subsequently phosphorylates a number of substrates inside the cell, collectively referred to as Insulin Receptor Substrates (IRS). When the cell is exposed to stress stimuli, this phosphorylation mechanism is inhibited, thus hampering insulin action on insulin sensitive cells⁹. However, in a study demonstrating the effect of psychological stress and sympathetic nervous system response on blood glucose showed that increased blood glucose in diabetes type II patients, as opposed to their weight and age-matched non-diabetic counterparts, was caused by increased hepatic glucose release rather than impaired absorption of glucose peripherally. This is in contrast to the established hyperglycemia-due-to-insulin-resistance hypothesis¹⁰.

Our study reported that males, more than females, were diagnosed for diabetes type II; of all the patients recorded to have high stress levels, males being almost double in majority. Females have been shown to have a "tend and befriend" response to emergency situations- which is a fostering response and has a propensity for decreasing stress levels. Whereas the "fight or flight" response has been implicated for both the sexes, males have shown greater tendency for such a response, possibly due to multifold greater testosterone levels – a major contributor to hyperlipidemia and insulin resistance. This proves to be the disrupting factor in the body's physiologic mechanisms and manifests itself as a disease¹¹. This however is in contrast to a study that showed plasma corticosterone shot up more rapidly in females than in males¹². Future studies should focus on the missing link to be identified. A major implication of the high stress levels in women however, especially in a Pakistani setup, such as social pressure to produce male babies, family pressure, house work pressure, etcetera, can also dissipate itself as feminization of male fetuses, studies show. This however may be independent of stress related diabetes as majority of the high stress level persons were of the age group 40 – 49, ruling out females to be in the reproductive age. Statistics demonstrate that a higher number of diagnosed people lie in the age group of 40-49. This demonstrates the hyperactive counteraction to stress by the HPA axis by people up the age ladder. Again, this chronic hyperactivity may provide clues to the development

of type II diabetes in our elderly subjects. Middle age is a time when the life of an individual might be filled with remorse over unaccomplished dreams, facing problems by their teen-age progenies. This emotional period can have significant impact on one's ability of stress management¹³.

Studies have been done that report stressful life events as a triggering factor for insulin-dependent type I diabetes during childhood¹⁴, suggesting that the release of cortisol, catecholamines and growth hormones during stress events lead to a baseline inflammatory condition of the body, triggering the development of type I diabetes. Interestingly, stress thus is a potent potential contributory factor in the development of both forms of diabetes. This proposes future research on mechanisms common to, and linking, the development of both diabetes I and II.

In our sample, interestingly, housewives ranked the highest amongst the diagnosed persons. However, a modest 49% reported of high stress levels. This suggests the possibility that lack of exercise and inactivity among the housewives can contribute to diabetes, taking its route via obesity rather than stress. The high stress levels housewives if coupled with obesity due to inactivity will be afflicted with an even higher risk for development of type II diabetes.

Psychosocial and socio-ecological stress among the different classes¹⁵ of our society accounts for the high stress levels in almost all of the subjects when assessed according to occupation, with only one government employee showing low stress level. Also, a whopping 100% doctors and 95% of the government employees diagnosed with diabetes were at high stress levels. This indicates that working conditions, non-payment of salaries, density of human population in their residences, and environmental factors which, along with genetic causes, are known to have a causative affect in the development of this multifactorial syndrome and contribute magnanimously to the buildup of stress among such individuals. Also, out of the 21 drivers diagnosed with diabetes, 18 (85.7%) indicated high stress levels, whereas a humble 3 demonstrated moderate stress levels.

Does genetic predisposition to diabetes lead to alteration in genetic structure that predisposes an individual to stress? Or is stress an independent causative factor of the metabolic syndrome? Our results here lower the balance moderately in favor of the latter question. 64.6% of the diagnosed people, along with a family history of diabetes, exhibited high stress levels. Studies addressing genetic predisposition to diabetes show that there may be sex linked relation in the inheritance of

type II diabetes and its causative metabolic defects. Also, a combination of family history, stress and resulting insulin resistance and visceral adiposity can lead to diabetes¹⁶.

Patients with diabetes type II should be in-tune with both their physical and psychological stress. Any stress will cause hyperglycemia, and a diabetic will have difficulty controlling the blood sugar once the blood sugar shoots up. Chronic high blood glucose levels are a predisposing factor to cardiovascular disease: coronary heart disease and debilitation of the microvasculature, leading to retinopathy, neuropathy and nephropathy.

The facts that exercise can increase the utilization of glucose by muscles even in the absence of insulin, and, cause the release of endorphins -“happy hormones”- to reduce stress can be related and used to curative advantage, and should be used in patient counseling; and to open a vast vista of therapeutic advancements in the management of diabetes type II. Intervention studies suggest that behavioral or pharmacologic intervention to manage stress may contribute significantly to diabetes treatment, but more long-term research is needed. It is concluded that further research is needed to establish the importance of behavioral factors in the etiology and management of diabetes, and several areas of methodological improvement are suggested¹⁷.

We also suggest intervention studies to reduce stress by developing stress models for individuals specifically in the Pakistani society and giving healthy alternatives to different working-statuses in the society under observed regimes. This may help to reduce stress and ultimately hamper its progression to take the form of diabetes and other disorders.

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Assessment of Change in Knowledge of Faculty After Attending A Workshop on Developing Integrated Curriculum

Bhavita Kumari¹, Salima Arif¹, Nighat Shah¹, Lubna Baig¹ and Shiraz Sheikh¹

ABSTRACT

Background: Integrated curriculum is defined as “intentional uniting or meshing of discrete elements or features [of a planned educational experience]”. There is a dire need for the educators to build integrated competency-based curricula. The rationale of the study is that there is a need to standardize capacity building trainings of medical faculty to acquaint themselves to the integrated curriculum. The objective of the study was to assess the change in knowledge of faculty after attending a workshop on developing integrated curriculum.

Methodology: A workshop for faculty was conducted in JSMU on Developing Integrated Curriculum. Data collection was done by two tools – pre- and post-questionnaire and evaluation form. Statistical analysis was done using Paired Samples t-test and McNemar Test.

Results: The number of participants considering the workshop as very good was 65.2%. Overall, there was a significant change in the mean total scores obtained by the participants’ from Pre-test as 3.61 ± 1.234 to Post-test as 4.61 ± 1.438 (p-value – 0.001).

Conclusion: The study concluded that there was a significant change in the mean total scores obtained by the participants. It is suggested to conduct frequent workshops for training of medical faculty and assess the change in knowledge, so that an integrated approach can be implemented in the medical curriculum.

Key words: integrated curriculum, syllabus, curriculum, SPICES

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عنوان: اساتذہ کا ایک تربیتی نشست برائے مربوط نصاب کی تعمیر پر تبدیلیئے معلومات کا تجزیہ۔

تحقیق کی وجہ: مربوط نصاب کی تعریف اس طرح کی جاتی ہے کہ منفرد اجزاء یا خصوصیات کی قصداً جمع کرنا یا مجال میں ڈالنا (جو منصوبہ بندی کے تحت تعلیمی تجربہ کی بنیاد)۔ وقت کی ضرورت ہے کہ ماہرین تعلیم اہلیت کی بنیاد پر ایک مربوط تعلیمی نصاب تربیت دیں۔ اس تحقیق کی وجہ استدلال یہ ہے کہ ایک نیا مربوط نصاب طب کے تعلیم کے لئے تیار کیا جائے۔

مقصد: اس تربیتی نشست کا حقدار شرکاء کو مربوط تعلیمی نصاب کی تعمیر کی تالیف سے آگاہ کرنا اور اساتذہ کرام کی معلومات میں اضافہ کرنا تھا۔

طریقہ کار: جناح سندھ میڈیکل یونیورسٹی میں اساتذہ کے لئے ایک تربیتی نشست برائے تعلیمی مربوط نصاب کا انعقاد کیا گیا۔ اعداد و شمار جمع کرنے کے لئے سوالنامہ جو شرکاء کو شروع اور آخر میں دیا گیا اور تجزیاتی فارم پر کرائے گئے۔ شماریاتی تجزیہ کے لئے Paired 't' test اور McNemar Test کا استعمال کیا گیا۔

نتیجہ: شرکاء کے 62.5% تعداد نے تربیتی نشست کو انتہائی مفید قرار دیا شرکاء کی ابتدائی اوسط معلومات اور تربیتی نشست کے بعد کی اوسط معلومات 3.16 ± 1.23 اور 4.61 ± 1.44 تھیں اور ان میں شماریاتی فرق ثابت ہوا ($P < 0.0001$)

حاصل مطالعہ: تحقیق سے ثابت ہوا کہ تربیتی نشست کی وجہ سے اساتذہ میں مربوط نصاب کی معلومات میں واضح اضافہ ہوا۔ یہ تجویز دی جارہی ہے کہ اس طرح کی مزید تربیت گاہوں کا انعقاد ہونا چاہیے اور شرکاء کی معلومات میں اضافہ کی تجزیہ ہونا چاہیے تاکہ مربوط تعلیمی نصاب کو بہتر طریقے سے طب کی تعلیم میں شامل کیا جائے۔

BACKGROUND

Integrated curriculum is defined as “intentional uniting or meshing of discrete elements or features [of a planned

educational experience]”¹. It is the organization of the curriculum, so that the interrelated subjects can be unified rather than being taught as separate modules. Integration is a vital component of modern approaches in curriculum development and renewal of higher studies especially medical education. It is a complex, comprehensive process demanding an intellectual approach to development, implementation, and assessment of a program curriculum. The essential constituents of an integrated curriculum are the

1 APPNA Institute of Public Health, Jinnah Sindh Medical University, Karachi, Pakistan.

Correspondence: Lubna Baig, APPNA Institute of Public Health, Jinnah Sindh Medical University, Karachi, Pakistan.

Email: lubna.baig@jsmu.edu.pk

horizontal associations between various subjects taught concurrently and the vertical associations between theories and practical approaches². The integration of curriculum aims to promote integrative learning, for example in medical studies to apply multi-disciplinary theories and skills to the patients' diagnosis and management. A multidisciplinary curriculum brings together all subjects related to a theme, making it a systemic approach rather than subject-wise approach. Therefore, it has been recognized as a critical educational methodology in medical education.

Syllabus and Curriculum are two different aspects of medical education. While the syllabus is a statement of content, curriculum is "all the courses of study offered by an educational institution"³. It is an extensive plan for education provision consisting of objectives, teaching strategies and assessment plan. SPICES model is defined as Student-centered, Problem-based, Integrated, Community-based, Electives, Systematic curriculum plan. It describes various educational methodologies useful in medical education⁴. The integration ladder is a useful tool for the medical teacher and can be used as an aid in planning, implementing and evaluating the medical curriculum⁵. Competency-based education (CBE) is an increasingly popular skeleton for developing curriculum focusing on learners' performance as an outcome⁶. The steps in curriculum planning include needs assessment, writing objectives, educational strategies, implementation and evaluation.

Competency-based education is directly applicable to ensuring accountability of the medical education endeavor as well as meeting the needs of medical students, patients, and the general public. The purpose of this workshop is to acquaint the participants with the skills of developing integrated competency-based curricula and enhance the knowledge of faculty regarding integrated curriculum.

There is a dire need for the educators to build integrated competency-based curricula. The new curriculum of medical studies is developed in integrated form. However, the faculty, new as well as senior, needs to adapt to the change by acquiring the knowledge on integrated curriculum. Therefore the rationale of the study is that, there is a need to standardize capacity building trainings of medical faculty to acquaint themselves to the integrated curriculum. The specific objective of the study was to assess the change in knowledge of faculty after attending a workshop on developing integrated curriculum.

METHODOLOGY

A workshop was conducted in Jinnah Sindh Medical University on Developing Integrated Curriculum. The audience consists of the senior faculty from Jinnah Sindh Medical University as well as its affiliated colleges.

Data Collection:

Data collection was done by two tools – pre- and post-workshop questionnaire and evaluation form. A pre-workshop knowledge Test was conducted before starting the workshop while a post-workshop assessed the knowledge after the workshop. Also, an evaluation form was filled by the participants' to evaluate the efficiency of the workshop. During the workshop, participants were imparted knowledge on difference between curriculum and syllabus, SPICES model, Integration ladder, Multidisciplinary Curriculum, Horizontal integration and Competency. They were also explained the various steps in Curriculum Planning.

Data Analysis:

There are 28 participants in the workshop; however, 5 participants did not take Post-workshop test. Therefore, 23 paired forms were entered into SPSS 16.0 for analysis and double checked. Statistical analysis was done using Paired Samples t-test for the total scores. Individual components of the workshop were assessed by McNemar Test.

RESULTS

The number of participants considering the workshop as very good was 15(65.2%) while an equal number of response was sought for good and excellent i.e., 5 each (21.7%). The number of participants saying that the concepts learnt could be applied to their institutes was 12(52.2%), while 11(47.8%) negated the statement. The assessment of individual components of the workshop can be seen in the tabular form. (See Table 1)

The participants' change in knowledge about Integrated Curriculum was assessed by a Pre- and Post-Workshop test. Overall, there was a significant change in the mean total scores obtained by the participants' from Pre-test as 3.61 ± 1.234 to Post-test as 4.61 ± 1.438 (p-value – 0.001). Participants' knowledge on syllabus inclusion significantly improved from 12(52.2%) participants knowing the correct answer before workshop to post-workshop as 20(87%) (p-value – 0.039). Participants' concept of competency improved significantly from 11(47.8%) to 18(78.3%) after the workshop (p-value – 0.016). Participants were also imparted knowledge about curriculum inclusion, SPICES model, Integration Ladder, multidisciplinary

Table 1: Participants’ evaluation of the Integrated Curriculum Workshop (n = 23)

		Good n (%)	Very Good n (%)	Excellent n (%)
1.	Presentation well-organized	7 (30.4)	13 (56.5)	3 (13)
2.	Objectives appropriate	7 (30.4)	11 (47.8)	5 (21.7)
3.	Content addressed objectives	9 (39.1)	9 (39.1)	5 (21.7)
4.	Workshop learning objectives were useful	5 (21.7)	12 (52.2)	6 (26.1)
5.	Presenter’s knowledge of the topic	2 (8.7)	7 (30.4)	14 (60.9)
6.	Presenter’s communication abilities	2 (8.7)	11 (47.8)	10 (43.5)
7.	Presenter’s response to questions/comments	5 (21.7)	10 (43.5)	8 (34.8)
8.	Usefulness of handouts/ presentation materials	2 (8.7)	11 (47.8)	6 (26.1)
9.	Workshop enhanced my learning	1 (4.3)	6 (26.1)	10 (43.5)
10.	Workshop objectives were achieved	7 (30.4)	12 (52.2)	4 (17.4)
11.	Over-all rating	5 (21.7)	15 (65.2)	5 (21.7)
12.	Concepts learnt can be applied to my institute		Yes 12 (52.2)	No 11 (47.8)

curriculum, Horizontal integration. However, the change in knowledge did not improve significantly. (See Table 2)

DISCUSSION

The study concluded that there was a significant change in the mean total scores obtained by the participants’ from Pre-test as 3.61 to Post-test as 4.61. Participants’ knowledge on syllabus improved from 52% participants before workshop to post-workshop as 87%. Similarly, their knowledge on concept of competency improved significantly from 48% to 78% after the workshop. Medical education workshops are conducted at all major medical schools to upgrade teaching modalities but their impact is usually not recorded. Therefore, the reliability and validity of the tool cannot be assessed and this is one of the limitations of the study is that the change in knowledge could not be compared with any previous literature.

Table 2: Pre- and Post-Workshop Comparison of Participants’ Knowledge about Integrated Curriculum. (n = 23)

	Pre-Workshop n (%)	Post-Workshop n (%)	p value*	
Syllabus Inclusion	12 (52.2)	20 (87.0)	0.039	
Curriculum Inclusion	9 (39.1)	14 (60.9)	0.062	
SPICES Model	11 (47.8)	15 (65.2)	0.344	
Integration Ladder	14 (60.9)	13 (56.5)	1.000	
Multidisciplinary Curriculum	13 (56.5)	12 (52.2)	1.000	
Horizontal Integration	10 (43.5)	8 (34.8)	0.687	
Competency	11 (47.8)	18 (78.3)	0.016	
Steps in Curriculum Planning	3 (13.0)	6 (26.1)	0.250	
Total Score	Mean	SD	t	p value**
Pre-Test	3.61	1.234	-3.649	0.001
Post-Test	4.61	1.438		

*p-value was calculated using McNemar Test

** p-value was calculated using Paired t-test.

It is suggested to conduct frequent workshops for training of medical faculty and the change in knowledge is assessed and reported. This way, standardized trainings can be developed to train the medical faculty to implement integrated approach in the medical curriculum.

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Hepatotoxic Effects of *Trichodesma indicum* n-hexane Extract in Mice

Nadia Parveen¹, Khwaja Zafar Ahmed², Zafar Saeed Saify³, Shafaque Mehboob² and Sajid Atif Aleem²

ABSTRACT

Objective: The aim of this study was to evaluate the hepatotoxic effects of *Trichodesma indicum* (whole plant) n-hexane extract in mice.

Method: The extract of the plant was given orally to 50 swiss albino mice for 15 consecutive days. At the end of the treatment period, evaluation of hepatotoxic effects was done on the basis of levels of liver enzyme markers such as alkaline phosphatase, alanin amino transferase, aspartase amino transferases and total bilirubin and histopathological examination of liver tissues.

Result: The plant extract significantly increased the liver enzymes and histopathological examination showed alteration in liver structure, vacuolation, karyorrhesis, pyknosis, chromatolysis and necrosis.

Conclusion: We conclude that the n-hexane extract of *Trichodesma indicum* can produce hepatotoxic effects; thereby, precautions should be taken during its traditional therapeutic use.

Key words: *Trichodesma indicum*, n-hexane extract, hepatotoxicity.

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عنوان: چوہوں میں *Trichodesma indicum* n-hexane جڑی بوٹی کی نچوڑ کی وجہ سے ہپاٹوٹاکسک زہریلے اثرات۔
مقصد: اس تحقیق کا مقصد چوہوں پر *Trichodesma indicum* n-hexane درخت کے عرق کی وجہ سے جگر پر زہریلے اثرات کا تجزیہ کرنا تھا۔
طریقہ: درخت کا نچوڑ تیار کر کے 50 (swiss albino) کو مسلسل 15 دنوں تک پلایا گیا۔ تجربہ ختم ہونے کے بعد ان خوراک کے زہریلے اثرات جگر میں موجود خامرہ (enzyme) کی تحقیقاتی عمل جیسے کہ alkaline phosphatase اور نسجوں میں تبدیلیوں کے مشاہدے (histopathological) کے ذریعہ کی گئی۔
نتیجہ: درخت کے نچوڑ نے جگر کے خامروں میں شماریاتی فرق کے ساتھ اضافہ کیا۔ ان خامروں نے جگر کی بناوٹ میں خالی داری، karyorrhesis, pyknosis, vacuolation, chromatolysis اور زندہ ٹیلیوں میں کی (necrosis) میں تبدیلی لائے۔
حاصل مطالعہ: اس تحقیق نے ثابت کیا کہ *Trichodesma indicum* n-hexane درخت کے نچوڑ کے استعمال سے زہریلے اثرات ہوتے ہیں۔ اس لئے اسے دوائی کے طور پر استعمال کرتے ہوئے احتیاط کرنی چاہیے۔

INTRODUCTION

Number of pharmacological and chemical agents are responsible for liver injury or hepatotoxicity such as poisons, toxins and herbal products etc¹. Some classes of drugs that are available for treatment of different

diseases causes hepatotoxicity such as anti-metabolites (methotrexate, 5-flourouracil and azathioprine), antibiotics (lincomycine, sulphonamides, ampicillin, tetracycline, erythromycin), beta blockers (propranolol), anti-inflammatory and pain relievers (phenylbutazone, ibuprofen, aspirin, indomethacin), oral hypoglycemic (chlorpropamide and tolbutamide), anti depressant (monoamine oxidase inhibitors and tricyclic anti-depressants), anti-tubercular agents (rifampicin, and isoniazid) etc². Some herbal products such as *Echinacea angustifolia*, *Echinacea pallid*, and *Echinacea purpurea* (*Echinacea*) that act as anti-infective should also not be used with hepatotoxic drugs³.

Trichodesma indicum synonyms are *Borage indica* L and *T.hirsutum*, is annual herb with hairy and spreading branches, belongs to *Boraginaceae* family. It has worldwide distribution in Afghanistan, Pakistan, India,

1. College of Pharmacy, Government College University, Faisalabad, Pakistan.

2. Institute of Pharmaceutical Sciences, Jinnah Sind Medical University, Karachi, Pakistan.

3. H.E.J. Research Institute of Chemistry, International Centre for Chemical & Biological Sciences, University of Karachi, Pakistan.

Correspondence: Shafaque Mehboob, Institute of Pharmaceutical Sciences, Rafiqi H.J. Shaheed Road, Karachi-75510, Pakistan.

Email: shafaque.mehboob@hotmail.com

Mauritius and Philippines⁴. It is used as alexeteric, emollient, thermogenic, anodyne, anti-inflammatory, constipating, depurative, ophthalmic, pectoral and febrifuge. Medicinally it is used in inflammation, diarrhea, dysentery, dyspepsia, dysmenorrhea, skin and urinary diseases and strangury. Leaves are effective in snake bite^{5,6}. Flowers acts as sudorific and pectoral⁷, used in sedation⁸. It is reported that whole plant methanolic extract of *T. indicum* acts as cough suppressant in Swiss albino mice⁹, anti-inflammatory¹⁰, anti-diarrheal¹¹, analgesic and antipyretic¹². The aim of this study was to evaluate hepatotoxic activity of n-hexane extract of *Trichodesma indicum* in Swiss albino mice.

MATERIALS & METHODS

Collection and identification of plant: *Trichodesma indicum* fresh whole plant was collected from the fields in Taxila, in the month of April. The plant *Trichodesma indicum* was compared with voucher specimen no: 254-1-13, deposited at Botany Department Herbarium at University of Agriculture Faisalabad.

Preparation of plant extract: the plant was washed with tap water; shade dried, powdered and soaked in the n-hexane extract for seven days. the extract was prepared by simple maceration process using 10L of solvent. The extract was evaporated under reduced pressure using a rotary evaporator at 65° C. the concentrate was stored at 4 °C in a dark amber colored bottle¹².

Experimental animals: Healthy adult albino female mice (25-30g) were used for the study. The animals were purchased from National Institute of health Sciences Islamabad. All animal were kept in standard plastic mice cages with stainless steel coverlids at animal house Government College University, Faisalabad, Pakistan. The animals were facilitated with the standard environmental condition of photoperiod (12:12h dark : light cycle) and temperature (25±2°C), with freely commercial mice feed. The food was withdrawn 18-24h before experiment though water was given ad libitum¹³.

All studies were conducted according to the standard guidelines of Ethical committee Government College University, Faisalabad and were approved by Advanced Studies and Research Board.

Experimental design: The animals were divided into control (group I) and four treated groups (group II- V). Ten animals were placed in each group. Group I received only vehicle olive oil (1 ml/kg/day orally) for 15 days. Plant extract was administered to remaining four groups by the same route of administration. Group II received

500mg/kg/day, group III received 1000mg/kg/day, group IV received 2000mg/kg/day and group V received 4000 mg/kg/day respectively.

Selection and preparation of dose for pharmacological screening: the n-hexane extract of the plant was suspended in olive oil to prepare four doses of 500, 1000, 2000 and 40100mg according to animal weight.

Preparation of stock solutions: for 500 mg/kg of plant extract, by dissolving 50 mg of plant extract per one ml of olive oil the stock solution was prepared; dose was administrated as 1ml/100mg. For plant 1000mg/kg dose of each plant extract, 100mg of plant extract was dissolved per 1ml of olive oil. Similarly 2000 and 4000 mg/kg of plant extract was prepared by dissolving 200 and 400mg of plant extract per 1ml of olive oil respectively.

Statistical analysis: the result was presented as mean+ S.D., and the statistical significance between the groups was analyzed by means of the analysis of variance (one way ANOVA).

Biochemical investigation: After fifteen days experiment was ended and 24h of the last dose, mice were anesthetized with chloroform and blood was collected by slaughter method. At room temperature blood samples were clotted for 45 min and by centrifugation at 2500 rpm for 15 min serum was separated¹⁴.

RESULTS

In control group, ALT value was 32.60+1.673. At dose of 500, 1000, 2000, 4000 mg/kg ALT level increased in dose dependent manner i-e, 40.00+0.1, 48.20+5.67, 56.80+2.168 and 60.60+1.949 respectively as shown in table-1.

The value of AST found in control group was 13.80+1.304U/L and it also displayed dose dependent increased in values i-e, at dose of 500 1000, 2000, 4000 mg/kg increased in AST values were 15.0+0.00, 16.00+3.94, 17.600+1.673 and 19.60+2.61

ALP value in control was 243.4+1.52 whereas, in doses of 500, 1000, 2000 and 4000mg/kg ALP values increased gradually from 337+13.51, 345+7.47, 356.6+3.13 and 392.60+0.0837 respectively.

Mean + SD used to show the results; the results were compared by one way ANOVA and the values were statistically significant p<0.001.

There was no marked change in bilirubin, albumin, protein and globulin values. Albumin value in control group was 3.740+0.894 which decreased to 3.30+0.100, 3.120+0.1095,

Table-1. Effect of treatment with *Trichodesma indicum* n-hexane extract on biochemical parameters.

Dose mg/kg	Control (n=10)	500mg (n=10)	1000mg (n=10)	2000mg (n=10)	4000mg (n=10)
ALP(U/L)	243.4±1.52	337±13.51	345±7.47	356.6±3.13	392.60±0.0837
ALT(U/L)	32.60±1.673	40.00±0.1	48.20±5.67	56.80±2.168	60.60±1.949
AST(U/L)	13.80±1.304	15.0±0.00	16.00±3.94	17.600±1.673	19.60±2.61
Bilirubin total	0.940±0.0894	0.740±0.0548	0.820±0.2049	0.600±0.100	0.680±0.837
Albumin	3.740±0.894	3.120±0.100	3.140±0.1342	3.180±0.0447	3.1600±0.0548
Protein	6.92±0.0837	6.820±0.1304	6.560±0.251	6.600±0.1732	6720±0.10952
Globulin	3.10±0.070	3.420±0.1643	3.340±0.2049	3.58±0.1643	3.10±0.070

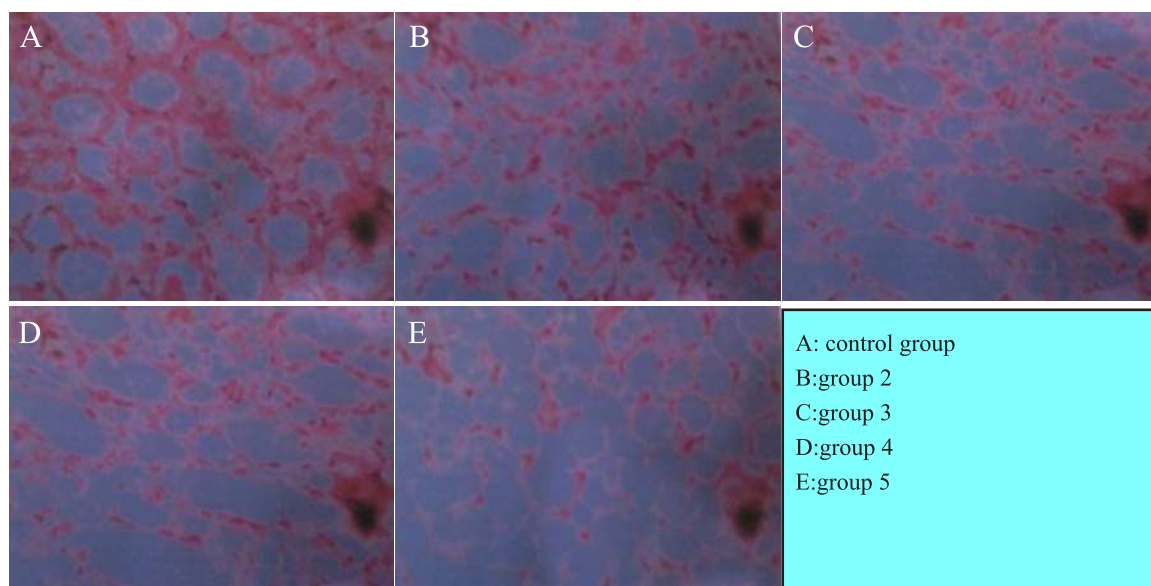


Figure -1: histopathology of liver section in control (A) and treated groups (B-E).

The group treated with extract displayed higher liver injury in histopathological examination as compared to the control group but maximum at 4000mg/kg dose as shown in fig-1.

DISCUSSION

Oral administration of n-hexane extract of whole plant extract of *T.indicum* given in doses from 500 to 4000mg/kg: showed no significant change in physical behavior, sensory nervous system responses, breathing, cutaneous effect, and gastrointestinal effects in female mice. All of the above effects were observed during the treatment period of 24 h but no death occurred in any of the groups. From this it was concluded that the single dose of the extract showed no adverse effects of *T.indicum*, signified that medium lethal dose (LD50) is higher than 4000mg/kg for female mice¹⁵.

Increased in AST level in blood may be due to hepatocytes damage and it has been used for measuring

liver necrosis. Increased in serum ALP as shown by 4000mg/kg dose of the extract may be measured as susceptible indicator of cholestasis in mild circumstances and earlier stages¹⁶. Liver produces aminotransferases (AST and ALT) which are good markers to indicate liver damage but no severity of damage necessarily¹⁷. Liver converts different exogenous compounds to inactive, less active or sometimes toxic metabolites that may lead to hepatotoxicity¹⁸.

Extract receiving groups 500,1000, 2000 and 4000mg/kg showed changes in mean of different parameters such as ALP, ALT and AST values but highest changes were observed at 4000mg/kg. however, no significant change was observed in globulin, bilirubin, albumin and protein values.

Figure shows the disappearance of hepatocytes, hydropic, degeneration, vascular degeneration, karyorrhexis, more prominent necrotic changes and chromatocytosis on dose dependant fashion.

Hepatotoxicity was produced by extract of *T.indicum* proved by altered biochemical parameters and histopathological examination attributed to the presence of pyrrolizidine alkaloids. In addition to this, as plants of the similar family also possessed hepatotoxic role, therefore, avoid unnecessary use of it as it may potentiate hepatotoxicity.

CONCLUSION

Trichodesma indicum (whole plant) n-hexane extract had shown elevated biomarkers of liver that proved its hepatotoxic effects as well as its histopathological studies also supported its harmful effects to hepatic tissues, therefore, cautions should be taken for the traditional use of *T.indicum* and further investigation should be done.

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Alpha-tocopherol and Ziziphus Jujuba as Mild to Moderate Hypolipidemic Agents

Khalid Niaz¹, Shahina Hakro², Amarlal Ghurbakhshani³, Abdul Qudoos¹ and Shah Murad¹

ABSTRACT

High plasma lipids, especially LDL-cholesterol, and low HDL-cholesterol in presence of or frequent formation of free radicals in various metabolic pathways in human body may lead to development of atherogenesis, CAD. Isomer of alpha tocopherol has antioxidant effects like other hypolipidemic drugs used in allopathy. Ziziphus Jujuba is medicinal plant having hypolipidemic potential. We conducted study on comparison of hypolipidemic effects of these two agents. Study was placebo-controlled conducted in Jinnah Hospital, Lahore from December 2015 to February 2016. Ninety hyperlipidemic patients were divided in three equal groups including 30 patients in each group. Their base line LDL-cholesterol and HDL-cholesterol was determined and kept in their personal file. Group-1 was on placebo, Group-2 was on Vitamin E 400 mg twice daily for two months. Group-3 was on half Kg Jujuba per day for two months. After two months therapy their post treatment LDL and HDL-cholesterol was determined. When analyzed statistically, results showed non-significant effects of herbal fruit/drug Jujube on HDL-cholesterol but significant role on LDL-cholesterol reduction. While vitamin E has highly significant reduction potential in LDL-cholesterol and significant effects on HDL-cholesterol with p-value <0.01. We concluded from the study that Z. Jujuba has antioxidant potential by lowering LDL-cholesterol in human plasma. But This effect is not comparable with hypolipidemic effects of Vitamin E as it also increases good cholesterol i.e. HDL-cholesterol.

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خون کی رگوں میں جسنے والی چکنائی دل کی کارکردگی میں رکاوٹ کی وجہ ہوتی ہے۔ کم کیت (LDL) والی چکنائی کی زیادتی ایسے کیمیائی مرکب کا باعث ہوتی ہے جو جسم کے تجزیاتی نظام میں بے قاعدگی پیدا کرتے ہیں۔ الفا ٹوکوفیرول جسم کے لئے غیر تکسیری کیمیائی اثر رکھتا ہے۔ Ziziphus Jujube ایک ایسا طبی خواص کا حامل پودا ہے جو جسم میں اثر پذیر چکنائی کے عمل کو متوازن کرنے میں مددگار ہوتا ہے۔ مقصد: اس تحقیق میں اس پودے کے خواص الفا ٹوکوفیرول کا موازنہ کیا گیا ہے۔ طریقہ کار: دسمبر ۲۰۱۵ سے ۲۰۱۶ فروری تک یہ تجربہ جینا ہسپتال لاہور میں کئے گئے۔ نوے مریضوں کو تین گروپ میں تقسیم کیا گیا۔ ہر گروپ میں ۳۰-۳۰ مریضوں کو رکھا گیا۔ سب سے پہلے کم چکنائی اور معتدل چکنائی کی جانچ کی گئی۔ اور تین فائل بنائی گئی۔ سب سے پہلے والے گروپ کو خالی بے ضرر ٹیبلٹ دی گئی۔ دوسرے گروپ کو وٹامن ای-۴۰۰ ملی گرام دو دفعہ دی گئی۔ تیسرے گروپ کو آدھا کلوگرام Jujube بوٹی کا پاؤڈر دیا گیا۔ دو مہینے بعد جانچ پر معلوم ہوا کہ Jujube بوٹی نے LDL کولسٹرول پر بہتر اثر کیا۔ نتیجہ: اس اس مطالعہ سے معلوم ہوا کہ Jujube بوٹی صرف LDL کولسٹرول کم کرتی ہے۔ اور وٹامن دونوں کولسٹرول یعنی LDL کولسٹرول کو کم اور HDL کولسٹرول کو زیادہ کرتا ہے۔

INTRODUCTION

Elevated levels of total cholesterol and low density lipoproteins (LDL) in plasma are major risk factors for the development of atherosclerosis¹. Much evidence provides support for the concept that the oxidized form of LDL causes oxidative stress and increases

intracellular Ca in the vessel wall, and represents the pathogenic element in hypercholesterolemia^{2,3}. Release of oxidant species from activated leukocytes, such as superoxide radical and hydroxyl radical, in principle, contributes to the oxidation of LDL. Thus, a strategy directed at the use of antioxidants such as vitamin E has been advocated to decrease the susceptibility of LDL to oxidation by interrupting free radical peroxidative chain reactions and to increase the resistance to atherosclerosis by protecting against endothelial dysfunction in hypocholesterolemic patients⁴. Vitamin E is lipid-soluble, chain-breaking antioxidant. Structural analyses have revealed that molecules having vitamin E antioxidant activity include

Pharmacology¹ / Biochemistry² / Physiology³, Islamabad Medical and Dental College, Islamabad, Pakistan.

Correspondence: Prof. Dr. Shah Murad, Department of Pharmacology, Islamabad Medical and Dental College, Islamabad, Pakistan.

Email: shahmurad65@gmail.com

four tocopherols ($\alpha, \beta, \gamma, \delta$) and four tocotrienols ($\alpha, \beta, \gamma, \delta$)⁵. One form, α -tocopherol, is the most abundant form in nature⁶. Alpha-Tocopherol is an important lipid-soluble antioxidant. It performs its functions as antioxidant in the glutathione peroxidase pathway and it protects cell membranes from oxidation by reacting with lipid radicals produced in the lipid peroxidation chain reaction. This removes the free radical intermediates and prevents the oxidation reaction from continuing. The oxidized α -tocopheroxyl radicals produced in this process may be recycled back to the active reduced form through reduction by other antioxidants, such as ascorbate, retinol or ubiquinol⁷. Vitamin E is transported in the blood by the plasma lipoproteins and erythrocytes. Chylomicrons carry tocopherol from the enterocyte to the liver, where they are incorporated into parenchymal cells as chylomicron remnants. The catabolism of chylomicrons takes place in the systemic circulation through the action of cellular lipoprotein lipase. During this process tocopherol can be transferred to high-density lipoproteins (HDLs). The tocopherol in HDLs can transfer to other circulating lipoproteins, such as LDLs and very low-density lipoproteins (VLDLs). During the conversion of VLDL to LDL in the circulation, some α -tocopherol remains within the core lipids and thus is incorporated in LDL. Most α -tocopherol then enters the cells of peripheral tissues within the intact lipoprotein through the LDL receptor pathway, although some may be taken up by membrane binding sites recognising apolipoprotein A-I and A-II present on HDL⁸⁻¹¹. Jujube fruit is known to contain considerable amount of phenolic compounds, including chlorogenic acid, gallic acid, protocatechuic acid and caffeic acid¹². It has been proved by researchers that level at which LDL oxidizes, decreases linearly with increasing phenolic concentration in plasma. Phenolic compounds are able to bind to LDL and this may account for the increase in LDL resistance to oxidation¹³. It is also possible that increases in HDL-cholesterol concentrations may contribute to the suppression of LDL oxidation and that polyphenolic compounds present in Jujubi may contribute to an elevation in HDL cholesterol¹⁴.

MATERIALS & METHODS

It was placebo controlled research study conducted in Jinnah Hospital, Lahore-Pakistan from December 2015 to February 2016. Ninety hyperlipidemic patients were enrolled in the study. Both gender male and female patients age range from 20 to 65 years were included. Written consent was taken from all participants and the study work on patients was approved by ethics committee vide reference letter no: JHL/RW-102 dated 29th November 2015. Their total cholesterol, HDL and

triglycerides were all measured directly and the LDL was calculated using the formula: $TC = LDL + HDL + (Triglycerides/5)$ ¹⁰. Separate Performa/file was made for every person. Patients suffering from any hepatic, renal or thyroid impaired disease were excluded from the study. They were divided in three groups, 30 individuals in each group. Group-1 was on placebo therapy i.e. advised to take one capsule (containing grinded wheat) thrice daily with each meal. Group-2 was on Capsule Evion 400 mg (containing Vitamin E). They were advised to take one capsule twice daily with their lunch and dinner. Group-3 was advised to take half kilograms dried, small size pulp of Jujuba in three divided times per day. All were advised to take their advised medicine for two months. Fortnightly clinic visit was advised to all participants. At the end of study we determined their lipid profile in the same Hospital Lab. SPSS version 26 was selected to determine and analyze change in the parameters. Mean values with \pm SEM were analyzed applying paired 't' test for determination of significance changes in parameters. P-value >0.05 was considered as non-significant change, p-value <0.01 was considered as significant and p-value <0.001 was considered as highly significant change in the parameter.

RESULTS

After two months therapy with Z Jujuba and vitamin E, it was observed that one patient withdrew from each group due to their personal reasons. When pre and post-treatment results were compared, it was observed that Vitamin E reduced LDL-cholesterol from 199.9 mg/dl to 187.7 mg/dl which is 12.2 mg/dl change in the parameter in 29 hyperlipidemic patients. When statistically analyzed this change was highly significant. HDL-cholesterol raised from 38.9 mg/dl to 45.7 mg/dl in this group which is 6.8 mg/dl increase in this parameter. It is significant change with p-value <0.01 . In group-3, LDL-cholesterol decreased from 190.1 mg/dl to 183.6 mg/dl. This decrease in tested parameter is significant with p-value <0.01 . HDL-cholesterol in this group increased from 40.6 mg/dl to 44.9 mg/dl in two months therapy by Z. Jujuba. Change in this parameter is 1.1 mg/dl, which is statistically non-significant with p-value >0.05 . In placebo group both parameters showed non-significant changes with p-values >0.05 , as shown in table:1.

DISCUSSION

Vitamin E molecules can interrupt free radical chain reactions by capturing the free radical. This imparts to them their antioxidant properties. The free hydroxyl group on the aromatic ring of vitamin E is responsible

Table showing pre and post-treatment values with their statistical significance in two months therapy by vitamin E and Z. Jujuba

Time/Group/change/SS	LDL-c	HDL-c
At day-0 G1 (n=30) G2 (n=29) G3 (n=29)	189.9±1.22 199.9±1.70 190.1±1.77	38.8±1.11 38.9±1.78 40.6±1.20
At day-60 G1 (n=30) G2 (n=29) G3 (n=29)	188.0± 1.91 187.7±1.17 183.6±2.10	38.6±1.71 45.7±1.11 44.9±1.29
Change G1 (n=30) G2 (n=29) G3 (n=29)	1.9 mg/dl 12.2 mg/dl 6.5 mg/dl	0.2 mg/dl 6.8 mg/dl 1.1 mg/dl
p-value G1 (n=30) G2 (n=29) G3 (n=29)	>0.05 <0.001 <0.01	>0.05 <0.01 >0.05

Key: G1= placebo group (n=30), G2= Vitamin E group (n=29), and G3= Jujuba group (n=29). 'n' stands for sample size. P-value >0.05 was considered as non-significant change, p-value <0.01 was considered as significant and p-value <0.001 was considered as highly significant change in the parameter. n=sample size. SS= statistical significance

for the antioxidant properties. The hydrogen from this group is donated to the free radical, resulting in a relatively stable free radical form of vitamin E. Vitamin E also reduces LDL-cholesterol. As in our results it decreased LDL-cholesterol 12.2 mg/dl in two months therapy for hyperlipidemic patients. JW chen et al., in 2012 proved almost same results. BN Wang et al., in 2010 stated mechanism of alpha tocopherol that it prevents oxidation of LDL particles and scavenges free radicals already formed in various tissues of human body. H Wang et al., in explained that when produced synthetically, it is composed of eight stereoisomers in which RRR- α -tocopherol is the most biologically active form which takes up and reacts with free radicals and may lead to form less toxic metabolites. J W Li et al., in 2013 proved that HDL cholesterol increase 8.15 mg/dl when 400 mg Evion (vitamin E) was used in 20 hyperlipidemic patients twice daily for three months. We proved 6.8 mg/dl increase in HDL cholesterol when 400 mg vitamin E was used in 29 hyperlipidemic patients. This contrast in results are due to their small sample size in their study. When half Kg Jujuba was used by 29 hyperlipidemic patients in our research work it was we proved that LDL cholesterol reduction was 6.5 mg/dl in two months therapy. HDL cholesterol increase in our result is non significant biostatistically in these patients i. e. 1.1 mg/dl. Results match with results of study conducted by Xuddan huang et al., in 2007 who proved 1.18 mg/dl increase in HDL cholesterol and 5.55 mg/dl decrease in LDL cholesterol. Same results proved studies conducted by GH Jagannadha Rao et al., in 2012 and SH Abd-Alrahman et al., in 2013 by using 600 grams Jujuba per day in

20 hyperlipidemic patients. AM Sabzghabae et al., in 2013 explained presence of various phytochemical compounds which act as antioxidant in human body preventing development of atherogenesis in human body. JW Li et al., in 2012 supported view points of AM Sabzghabae et al regarding presence of phytochemicals in various herbal plants and their hypolipidemic potential with lesser SEs.

CONCLUSION

It was concluded from this research study that Vitamin E is very potent antioxidant agent when used alone or in combination with herbal medications like Ziziphus Jujuba. Ziziphus Jujuba when used alone have more hypolipidemic effects on 'Bad' cholesterol i.e. LDL cholesterol but non-significant effects on Good cholesterol i. e. HDL cholesterol

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(Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication)

Primary Airway Management of Pediatric Supraglottic Stenosis

Syed Muhammad Tariq Rafi¹, Shafaque Mehboob^{1*}, Zafar Saify² and Maria Ahmed³

ABSTRACT

Pediatric supraglottic stenosis is a rare and unusual subset of laryngotracheal stenosis. Early intervention and careful endoscopic management help to achieve the best possible outcome and can reduce the mortality rate. We present the case of 8 years old boy who developed supraglottic stenosis after road traffic accident. Initially tracheostomy was done to relief the complications related to the narrowing of airway. After that, dilatation was done to remove tracheostomy. The procedure was performed under general anesthesia without any hazard. This primary airway management was followed by consultation of chest surgeon to get rid of blunt laryngeal complications, if any.

Conclusion: Endoscopic dilatation is the primary airway management for pediatric population in supraglottic stenosis at early stage but may require adjuvant therapy. Further details still need to be established for the management of this rare entity.

Key words: supraglottic stenosis, dilatation, rare entity.

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عنوان: بچوں میں پائے جانے والے سپر اگلوتک اسٹیونوسس (Supra-glottic stenosis) کیلئے ابتدائی طور پر سانس کی نالی کے ذریعے طریقہ علاج۔
طریقہ علاج: بچوں میں سپر اگلوتک اسٹیونوسس شاذ و نادر ہی پایا جاتا ہے۔ اگر ابتدائی علامات کے ظاہر ہوتے ہی بہترین اینڈواسکوپک طریقہ کار کو استعمال کیا جائے تو نہ صرف اس کے بہترین نتائج برآمد ہو سکتے ہیں بلکہ زندگی بچانے کے تناسب میں بھی اضافہ ممکن ہے۔ زیر مشاہدہ مخصوص بیماری کی کیفیت (Case report) میں ایک آٹھ سالہ لڑکے کے سپر اگلوتک اسٹیونوسس کی تفصیل بیان کیا جا رہی ہے جو کہ ٹریفک حادثے کے بعد نمودار ہوا۔ ابتدائی طور پر سانس کی تکلیف دور کرنے کیلئے tracheostomy ٹریکیسٹومی کی گئی جس کے بعد بناء کسی پیچیدگی کے کشادگی (dilatation) تلیک بروئے کار لا کر ٹریکیسٹومی کو ہٹایا گیا۔ حفظاً مقدم کے طور پر مریض کو سینے کے امراض کا وارڈ (Chest ward) سے رجوع کرنے کیلئے کہا گیا۔
نتیجہ: سپر اگلوتک اسٹیونوسس کیلئے کشادگی (dilatation) ابتدائی طور پر بہترین طریقہ کار ہے مگر اسکے باوجود اکثر اسکے ساتھ ساتھ دوسرے طریقہ کار کی بھی ضرورت پڑ سکتی ہے۔

INTRODUCTION

Tracheostomy is a common procedure in intensive to relief the complications associated with Laryngotracheal stenosis¹. Laryngotracheal stenosis is the narrowing of airway, be it glottis, subglottis and trachea but subglottic stenosis is the most common type of it². Supraglottic stenosis is an unusual

subset of laryngotracheal stenosis that has distinctly different causes, symptoms, and treatment options³. Usually balloon dilatation is considered as a method of choice in the treatment of laryngeal stenosis in children at early stage. The ultimately purpose of this procedure is to remove tracheostomy but under general anesthesia in children. Dilatation has less complication over other traditional open surgical methods and can reduce the worsening of clinical symptoms. In the case of subglottic stenosis it helps to achieve sufficient laryngeal lumen dilatation without any open operative procedure⁴.

In pediatric population, stenosis has to be managed with a wide range of innovative endoscopic methods such as serial dilatation, tracheostomy and reconstruction with proper observation. In early diagnosis is done, serial dilatation may create enough radial force that may prevent the open surgery without non-compromising complications in children⁵.

1 Jinnah Sind Medical University, Karachi, Pakistan.

2 H.E.J. Research Institute of Chemistry, International Centre for Chemical & Biological Sciences, University of Karachi, Pakistan.

3 Jinnah Post Medical College, Karachi, Pakistan.

Correspondence: Dr. Shafaque Mehboob Institute of Pharmaceutical Sciences, Jinnah Sindh Medical University, Rafiqui H.J Shaheed Road, Karachi 75510, Pakistan.

Email: shafaque.mehboob@hotmail.com

Case report:

An eight years old boy, resident of Sukkhar, Sindh, came via emergency of Jinnah hospital to E.N.T ward in 2016. He had road traffic accident before three months and had admitted in emergency department of the local area. He received the endotracheal tube during the treatment for prolong time. He was presented in the E.N.T ward with supraglottic stenosis. Initially, tracheostomy was conducted to relief the symptoms and complications associated with stridor temporarily. Scanning protocol includes T1 and T2 weight axial, coronal and sagittal images, obtained with I/V contrast. Findings showed that tracheostomy tube seen in situ at level of T1-T2 producing marked streak artifacts. There was circumferential narrowing measuring 0.8 cm seen in the region of supraglottic part of larynx resulting in significant luminal narrowing extending up to the anterior part of the glottic region, measured 1.4 cm craniocaudally. Infraglottic part appeared normal. There was absence of communication between the fourth ventricle and posterior fossa with abnormal extra CSF spaces in the posterior fossa region may be due dandy walker. No evidence of mass on either side of neck was present. The paroid, submandibular and thyroid glands as well as vascular structures were normal. That presented the case of supraglottic stenosis in the child.

As this rare case is life threatening, therefore, first of all tracheostomy was done to relief the child from problems associated with breathing. After that, it was planned to perform dilatation in order to improve the lumen diameter of larynx without performing open surgery. Since laryngeal strictures are shorter, therefore, in first dilatation catheter of 6.7 mm was used. This procedure was performed to get rid of tracheostomy or reinsertion. The patient was maintained on combinations of steroids and antibiotic and observed for a week in the same ward. The child seemed to be improved but was susceptible for lung obstruction, that's why he was referred to the chest ward.

DISCUSSION

Supraglottic stenosis is a rare complication with the variety of symptoms such as inspiratory stridor and feeding difficulty. Physical examination and history play important role in its diagnosis and to differentiate it from subglottic stenosis⁶. It is a challenging problem for otorhinolaryngologist and may require both endoscopic and open surgical processes^{7,8}. However, dilatation is the primary and safe method for the pediatric patients to manage this type of stenosis. It is usually performed under general anesthesia to remove tracheostomy without any significant complications and hence, to reduce clinical symptoms associated with narrowing of Laryngotracheal lumen⁹. In the case of recurrent of stenosis, balloon dilatation may require adjuvant therapy such as laryngoplasty¹⁰. However,

dilatation is the first choice for the most of the surgeons as it has high success rate. It reduced the symptoms temporarily in childhood supraglottic stenosis in 60% cases without open surgery and showed improvement in 60% of the case in a study done by Whigham A. S. et al. The chances of failure appear if the early complications appeared after first dilatation specially if it is performed alone. Some studies showed the success rate with additional procedure from 50% to 78%⁴.

Therefore, the author first prefers the relief of the breathing difficulty of the boy through the procedure of tracheostomy and then adopted the safe method of choice of dilatation to reduce the complications. Then keep the child under observation for a week during which he remained symptoms free. After that the patient was referred to the chest ward after 15 days to consult for further complication, if any.

CONCLUSION

Endoscopic dilatation is the primary airway management for pediatric population in supraglottic stenosis at early stage but may require adjuvant therapy. Further details still need to be established for the management of this rare entity.

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A Case Report on Infratemporal Fossa Growth; Excision with Surgical Expertise and Less Morbidity

Beenish Nisar Ahmed¹, Iqbal Hussain² and Muhammad Waqas Nisar Ahmed³

ABSTRACT

Neoplastic lesions of infratemporal fossa are presented with variegated pathologies. Lesions that involves the infratemporal fossa more often originate as a result of extension from neighbouring structures and from primary tissues of fossa as well. Metastatic lesions are also common. Because of its enshrouded location, usually tumors presents lately. Clinical signs and symptoms are insidious. The close proximity of the area to the intracranial structures, the orbit, the paranasal sinuses, the nasopharynx, and the facial area demand meticulous surgical excision. Modern imaging techniques have made three-dimensional visualization of the extent of the pathology possible. Radical tumor excision with preservation of the quality of life remains the ultimate goal. We report a rare presentation of infratemporal fossa growth. The patient underwent surgical excision and had uneventful recovery.

Key words: Infratemporal fossa, radical tumor excision

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عنوان: دماغ کے ٹیپورل حصے کی ٹیچلی سطح پر خردور و افراش کی با مہارت پیوند کاری اور دماغ کے دیگر حصوں کو دورانِ جراحی محفوظ رکھنا۔
ٹیپورل دماغ کے نچلے حصے پر ایک ایسی جگہ موجود ہے جہاں پر مختلف اقسام کی افراش (خردور و افراش) کے آثار ملتے ہیں۔ ٹیپورل کی ٹیچلی سطح کو جو چیزیں سب سے زیادہ متاثر کرتی ہیں، وہ یا تو برابر کے حصے والے امراض ہیں جو اس حصے تک پہنچ جاتے ہیں یا خردور و افراش ہیں۔ اس کے علاوہ دماغ کے دوسرے حصوں میں پیدا ہونے والے سرطان بھی اس جگہ پہنچ جاتے ہیں۔ کیونکہ یہ حصہ چھپا ہوا ہے اسی لئے یہاں پر موجود مرض کا آسانی سے پتہ نہیں چلتا۔ معالج بھی ظاہری تشخیص کے ذریعے اس کو آسانی سے پہچان نہیں پاتے ہیں۔ یہ حصہ، دیگر حصوں جیسے ناک کان اور چہرے سے ملا ہوا ہوتا ہے اس لئے یہاں ہونے والی افراش کو جراحی کے ذریعے نکالنا اتنا آسان نہیں ہے۔ جدید طریقوں کی مدد سے اس بات کو ممکن بنالیا گیا ہے کہ اس جگہ کی افراش کی تین راویوں (۳ ڈی) سے مکمل طور پر دکھایا جائے۔ مگر اصل مقصد افراش کو مکمل طور پر صاف کرنا ہے۔ اس خاص علاج (کیس) رپورٹ میں ہم ایک ایسا کیس پیش کر رہے ہیں، جس میں اس حصے میں پیدا ہونے والی افراش کی نہ صرف تشخیص کی گئی ہے بلکہ اس افراش کو مکمل مہارت جراحی سے نکالا گیا ہے اور ساتھ ہی مریض کے دماغ کے دیگر حصوں کو بھی محفوظ رکھا گیا ہے۔

INTRODUCTION

The infra temporal region because of its obscures location is in accessible for clinical examination. Thus lesions other than malignant rapid growth pattern type may continue their growth for longer period and symptoms appeared late. Radiological investigations are usually first to diagnose the disease¹.

Over decade various pathologies have been experienced in this area. Treatment of infratemporal growth depends upon the type and extension of disease. Basic aim is to clear the disease radically with less morbidity¹⁻³.

Primary tumors of infratemporal fossa include fibrosarcoma, haemangioma, Hodgkin s lymphoma meningioma, neurofibroma, rhabdomyosarcoma. Benign tumors include lipoma, maningioma, fibroma and schwannoma. Malignant tumors include adenoid cystic, adenocarcinomas and fibrosarcoma¹⁻⁵.

In our literature review Conley, shapsshay and shaheen provided that majority is of primary tumors²⁻⁸.

Adenoid cystic carcinoma is the most commonly occurring malignant tumor. Indolent growth pattern leads to delayed diagnosis and late presentation. Sign and symptoms occurred according to the spread of

1 Department of ENT, Shifa International Hospital, Islamabad, Pakistan.

2 Department of ENT, Civil Hospital Karachi, Pakistan.

3 Jinnah Sindh Medical University, Karachi, Pakistan.

Correspondence: Dr. Muhammad Waqas Nisar Ahmed, Lecturer and Member of Medical Examination Committee, Jinnah Sindh Medical University, Rafiqui H.J Shaheed Road, Karachi 75510, Pakistan.

Email: drwaqasnisar@yahoo.com

tumor to surrounding structure i.e. nasal, ear and facial symptoms etc.⁵⁻⁶ Approaches to infratemporal fossa are multiple and needs surgically experience hand . Prognosis is highly influenced by the nature of disease and completeness of the resection³⁻⁵.

Case report

10TH Jan, 2014

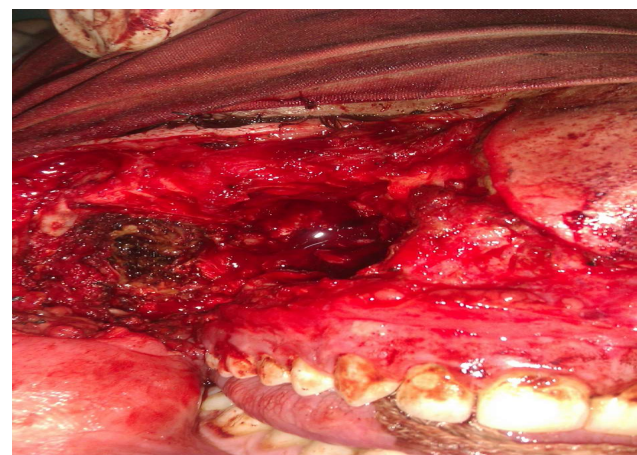
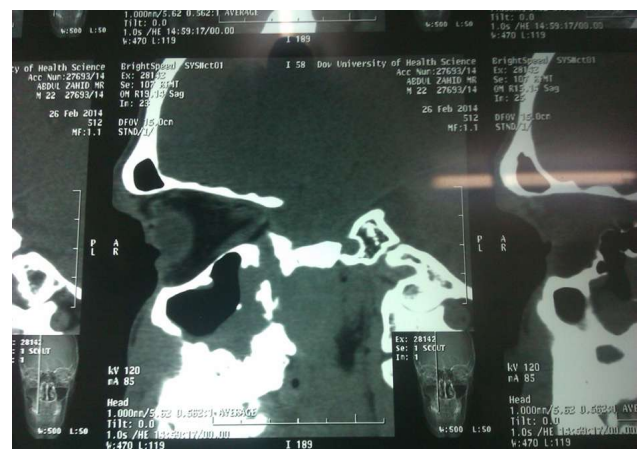
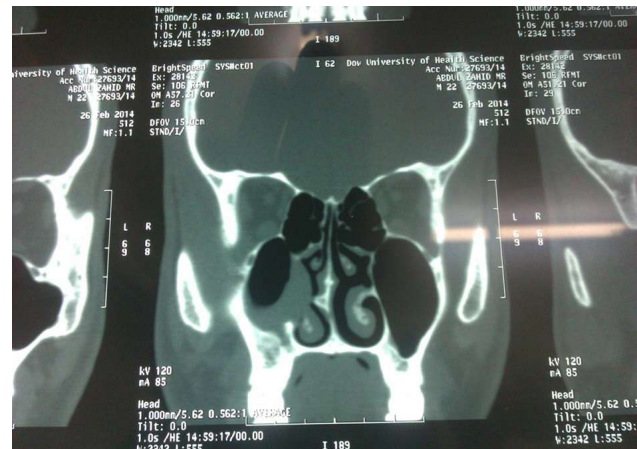
Federal clinic hospital, Karachi, Pakistan

22 Years, male

CR no 31/03

22 years old male presented to us with restricted mouth opening and difficulty in chewing for last three months. He is also complaining of reduced hearing from right ear for the same duration. His history was not significant for any other symptoms. Upon examination he was young, healthy, active and well oriented male. His other systemic examination was unremarkable. His local examination showed right ear conductive deafness and trismus with mouth opening one finger breadth. Other examination was unremarkable. His base line haematological investigations were normal. His CT showed soft tissue mass in right infratemporal fossa, 3.8x4.6x4.7 cm in AP,CC,TR dimensions. It was involving masticator muscles with loss of muscle plane. Anteromedially it was causing destruction of lateral pterygoid plate and, laterally extending to right maxillary sinus thinning of ramous of mandible due to bony erosion. Mass was also extending in to ptrygomaxillary fissure to reach the lateral wall of right nasal cavity and superiorly it was abutting the base of right middle cranial fossa ,inferiorly involving pterygoid muscles, posteriorly abutting the Para pharyngeal fat and parotid gland. The mass lesion show no significant enhancement. The findings were suggestive of euplastic lesion of infratemporal fossa.

Surgical excision was planned .Informed consent have been taken. Patient underwent excision of growth via anterior transfacial approach using Weber Ferguson incision. Mass was extending from lateral pterygoid plate to maxillary sinus ,nose lateral wall and abutting right middle cranial fossa. Lesion was resected completely but not in toto as the growth was firm tissue. Mass removal was not easy because of extension, surrounding vital structures and suspected bleeding . Lesion was cleared from its lateral, posterior, anterior and medial margins until normal tissue reached .Middle cranial fossa was also saved and no major vessel bleeds. It was not a vascular growth. After resection cavity was packed. Post operative recovery was uneventful and patient was followed on regular basis. The histopathology report showed Fibroma, benign growth



of infratemporal fossa .Patient recovered completely and he was on regular follow-ups with repeat CT scans and showed no recurrence .Patient symptoms were also improved .Mouth opening size increased, hearing and chewing improved.

CONCLUSION

Infratemporal growth are difficult to handle per operatively because of the vital surrounding structures. It needs surgically experience hand to excise completely and providing less morbidity to patient. In this case what we found is the late presentation, extensive but benign lesion. Not easily but resectable completely with gentle care and skilled techniques per operatively.

DISCUSSION

The infratemporal fossa is an irregularly shaped cavity, situated below and medial to the zygomatic arch. Boundaries involved *anteriorly*, by the infratemporal surface of the maxilla and the ridge which descends from its process, *posteriorly*, by the articular tubercle of the temporal and the spina angularis of the sphenoid, *superiorly*, by the greater wing of the sphenoid below the *infratemporal crest*, and by the under surface of the temporal squama, containing the foramen, which transmits the mandibular branch of the trigeminal nerve, and the foramen spinosum, which transmits the *inferiorly*, by the medial pterygoid muscle attaching to the mandible, *medially*, by the plate and *laterally*, by the ramus of mandible, which contains the , leading to the through which the passes. This also contains the lingula, a triangular piece of bone that overlies the mandibular foramen antero-medially. Finally, the mylohyoid groove descends obliquely transmitting the the only motor branch of the posterior division of the nerve. Muscles found in this area are Lower part of the Temporalis and masseter muscles (origin of masseter muscle: lower margin of the inner surface of zygomatic bone insertion: outer surface of the ramus of the mandible) and muscles. Internal maxillary artery branches found within the infratemporal fossa including inferior and deep artery. Pterygoid venous plexus is the vein found there¹⁻⁵.

Nerves involve Mandibular nerve, inferior alveolar nerve, lingual nerve, buccal nerve, chorda tympani nerve, and otic ganglion⁷⁻⁹.

The foramen ovale and open on its roof, and the alveolar canals on its anterior wall. At its upper and medial part are two fissures, which together form a T-shaped fissure, the horizontal limb being named the inferior orbital, and the vertical one the pterygomaxillary⁴⁻⁶⁻⁹.

Approaches to temporal fossa are multiples and involve surgical expertise. Approaches includes anterior trans facial approach using Weber Fergusson incision, transorbital, trans pterygoid, transantral, transpalatine extended maxillotomy, maxillary swing, transoral via gingivolabial sulcus, preauricular transzygomatic, trans cranial, transmandibular facial degloving, preauricular transtemporal, recently endoscopic approach are also gaining popularity³⁻⁵.

Prognosis of disease is depended upon the final histopathology of tissue.

In this case a young male presented with huge extensive growth but fortunately turn out benign and resected completely with good prognosis. The important aspect is the per operative surgical technique used to clear disease and the patience to clear it completely saving all vital surrounding structures.

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Pressure Sores in Healthy Physically Active Person: A Rare Presentation

Aisha Siddiqui¹, Khalid Rashid² and Mariam Asif¹

ABSTRACT

Pressure sores are one of the common manifestations in bedridden patients or with chronic illnesses. They usually occur over bony prominence. Prevalence, risk factors include reduced mobility, impaired sensations as in diabetes, spinal cord injuries, chronic illness like immobility, extremes of age, vascular diseases, malnutrition and dehydration. We report a case of pressure sores on the gluteal region in a patient with no co-morbid disease or significant risk factor. A 45 years old male presented with infective ulcerations on both gluteal regions along suppuration of right inguinal lymph nodes. In this case, Imaging studies, like sinogram and magnetic resonance imaging were useful, but histopathology played the decisive role in the proper diagnosis.

Key Words: Pressure sores, Prevalence, Sinogram, risk factors

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عنوان: صحت مند اور جسمانی طور پر سرگرم فرد میں دباؤاتی زخم (Pressure sores): ایک کمیاب مریض

دباؤاتی زخم عام طور سے مستقل بستر پر لیٹنے والے یا مزمن (Chronic) مریضوں میں پایا جاتا ہے۔ یہ عام طور سے ان افراد میں ہوتا ہے جن کی ہڈیاں ابھری ہوئی ہوتی ہیں۔ جسمانی حرکت میں لمبی معذوری کا احساس ریڑھ کی ہڈی کا زخمی ہو جانا، مزمن امراض، عمر رسیدگی، نسیلا (Vascular) امراض، خوراک یا پانی کی کمی عام طور سے اس بیماری کی وجہ یا اس کے پھلاؤ کی وجہ جانتے ہیں۔ ہم اس پرچہ میں دباؤاتی زخم پر ایک case جو Gluteal region میں تھا پیش کرتے ہیں۔ اس مریض میں اس سلسلہ کی کوئی اور بیماری نہیں تھی۔ اس مریض کی عمر 45 سال تھی اور اس کے Gluteal region کے دونوں حصوں میں زخم کے علامات پائی گئیں۔ اس طرح کے علامات میں تصویریری تشخیص کی جاتی ہیں لیکن histopathology (نسیوں میں تبدیلیوں کا مشاہدہ اور مطالعہ) ہتمی تشخیص کرتی ہے۔

INTRODUCTION

Pressure Sores may be defined as 'skin ulcerations' due to pressure in combination with the effect of other variables¹. They are thought to be caused by combination of pressure, shear and friction². Seventy percent of the pressure sores occur in persons over age seventy³. Its incidence vary widely by clinical settings^{4,5}. Commonly affected sites comprising approximately eighty percent of the wound, are pelvic girdle (lower portion), Sacrum, coccyx (tail bone), trochanter and

heel³. Pressure ulcer always occur in those identified bony areas where tissue destruction is highest⁶. There are certain conditions that affect flow of blood through the body such as type 2 diabetes. It predisposes a patient to many conditions including pressure sores³. We here, present a rare case of a 45 years old watchman who developed pressure sores on his both sides of buttocks with no significant risk factors.

Case Presentation:

A 45 years old male watchman by profession, presented to the outpatient department of government hospital Karachi, Pakistan with the complaint of painful swelling in the right gluteal region for last 2 years that ruptured spontaneously. A few days later same swelling appeared over a left gluteal region, which also ruptured impulsively. The patient also had pain and itching in the particular region associated with discharge. Discharge contain pus and blood almost few drops to one and half teaspoon in quantity. Six months before,

1 5th year Medical Student, Sindh Medical College.

2 Department of General Surgery, Jinnah Postgraduate Medical Centre, Karachi, Pakistan.

Correspondence: Aisha Siddiqui, Sindh Medical College, Jinnah Sindh Medical University, Rafiqi H.J Shaheed Road, Karachi 75510, Pakistan.

Email: aishasiddiqui034@gmail.com

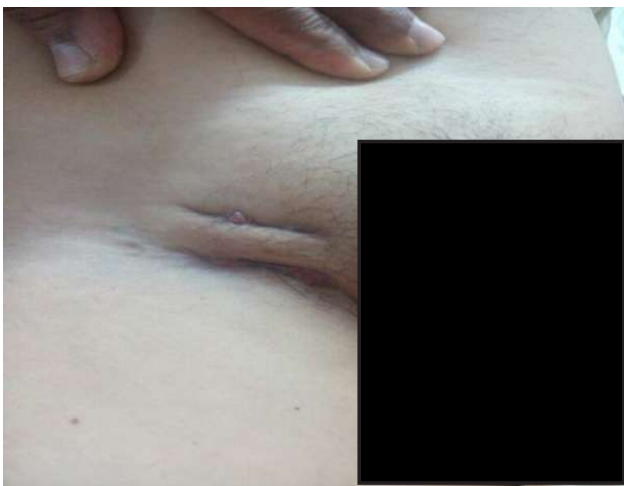


Fig 1 & 2: Respectively showed healed lesions (photograph).



Figure 3 & 4: Respectively: Control film sinogram.

he had same swelling in the right inguinal region. It was most probably due to blockage of the lymphatic drainage from the buttock region with suppuration. Incision and drainage was done. Postoperatively the patient had pain and bleeding from wound followed by pussy discharge.

There was no history of local injection in the buttock prior to presentation. Family history was positive for tuberculosis.

On General Physical Examination, a middle aged male normal built and vitally stable. Signs of jaundice, dehydration, anemia, and cyanosis were absent. A local examination showed multiple discharging sinuses like pits over gluteal regions with swelling over the right inguinal region. On investigation

CBC: Hb:13.2g/dl, WBC:8.3x10⁹, PLT:261x10³/uL, INR:0.6, PT:8.7sec, APTT:27sec, Na:136mEq/L, K:4.1mEq/L, Cl:100mEq/L, RBS:116mg/dl, Urea:26mg/dl, Creatinine:0.8mg/dl, ESR-96mm/1st hr.

Chest x-ray was normal. Empiric anti cox therapy was started with the assumption of tuberculosis. Pus for culture and sensitivity was sent that showed E. coli. We performed three phase skeleton scintigraphy to diagnose any bone disease. The findings were within normal limits. MRI scan of gluteal region was ordered to further characterize and define the extent of this swelling. A linear tubular high intensity area noted within deep fibers of gluteus maximus muscle medially which is extending upwards and anteriorly in close proximity of the right quadratus femoris and ending blindly in right ischioanal / ischiorectal fossa. Maximum width of 1.1cm and cranio-caudal extent is approximately 4.3cm.No communication with sigmoid colon and rectum. Another high intensity signal area noted within soft tissue of right inguinal region anterior to right pectineus and medial to right sartorius muscle measuring 1.9x1.7cm.Two sub centimeter size lymph nodes noted along right internal iliac chain and single small one along left internal iliac chain. For further evaluation sinogram was performed (figure3 &4) that showed no definitive communication between bowels and bones with the skin.

We made a differential diagnosis of granulomatous inflammation (tuberculosis) and infected pressure sores. To rule out tuberculosis, we did a biopsy twice that revealed granulation tissue infiltrated with neutrophils, lymphocytes, Plasma cells and foamy histiocytes. No granuloma nor malignancy is seen. Thus the biopsy confirmed the pressure sores. We stopped Anti cox 1 therapy for Tuberculosis and he was then advised for nutritional work-up. Proper debridement of damaged tissues along with proper wound care was done in this patient and for prevention of infections antibiotics were given. Topical preparations were given to prevent further tissue damage. The patient was counseled properly regarding the illness as reduction of pressure in that area is of very much significance.

DISCUSSION

High risk factors for developing pressure sores are immobility, poor nutrition, corticosteroids use, and any debilitated disease like diabetics, psychological impairments, dehydration and infections³. Surprisingly, our patient developed sores without any predisposing factors.

Pressure sores may result from skin friction against any hard surface. It can result from prolonged sitting over hard surface of the seats or bed that exerts excessive pressure on the bony prominence or pressure points on the body. Local ischemia followed by cell damage can be a consequence. Common pressure points in the body include Sacrum, Coccyx, ankle and heel³. In our case, we were suspecting his occupation of watchman as a possibility, but he completely denied prolonged sitting.

According to published studies pressure sores can be the result of shearing forces, friction and moisture while lying². However Patient in this case was healthy and used to perform all normal physical tasks. Kataria et al⁷ reported a case of a diabetic paraplegic patient who had multiple bed sores involving sacral areas, heel and bilateral popliteal fossa. He concluded that pressure sores are the frequent complication of spinal cord injury and an important cause of hospitalizations. Nutritional status is an essential factor in the greatest tissue healing and the development of increased immunity against infections Holmes et al⁸. We assessed our patient's diet which included adequate amount of carbohydrates, fats and proteins.

Age is one of the important risk factors for development of sores due to poor blood supply and wound healing in an elderly patient⁹. According to the study conducted in MOH (1998) 78% of the cases of pressure sores

were above the age of 60¹⁰. While some studies suggested that pressure sores occur after age seventy³. In this case the patient's age is 45 years, which is less likely to be the risk factor.

A micro vascular disease caused by diabetes and loss of sensations in the lower part of the body contributes to the development of pressure sores^{1,3}.

A source of pressure identification is an essential step for the prevention of recurrence. When the patient's overall health supports healing still no improvement noted, the source of pressure may not be correctly identified, therefore intervention may not be effective.

CONCLUSION

Individual risk assessment plays an important role in the pressure sores, development, further management and prevention of sores. Pressure sores/ ulcers usually occur due to one or more predisposing factors mentioned above. It's important to identify and treat. However some cases may have rare presentation without any predisposing factors. It's important to counsel and aware the patient about proper management along with postural changes.

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Role of Pharmacist in Health Education

Khwaja Zafar Ahmed¹ and Shafaque Mehboob¹

Pharmacy as a profession has yet to achieve in Pakistan a status which it enjoys in all developed countries. This is particularly unfortunate in view of the fact that it is in a country like Pakistan that Pharmacy requires to be but on more healthy and regulated basis as developed countries can look after a number of their problems particularly in the field of health, in a variety of other ways. Here, in Pakistan, the need is great, the problem is immense, the resources meager and the effort restricted¹.

What role has a pharmacist to play in Health Education? This question it appears that has never occurred to our doctors, public health experts and social workers. It would be worthwhile knowing that by ignoring pharmacists one would leave out health centers spread out in the most towns and villages and every city and pharmaceutical manufacturing establishments through which health education can be projected. So important is this role of the pharmacist as health educator that a special session of the International Pharmaceutical Federation has directed its attention to what they call this "application of services".

The scope and potentialities of this service are truly tremendous. It the pharmacist and the chemist shop to whom majority of the patients and a very large number of health persons go for their requirements. More often not advice is sought from the pharmacist on matters of minor ailments, aches, pains, headache and worries. Surely there is ready opportunity at that stage that a pharmacist who is qualified person in various scientific subjects including Hygiene, can give advice to the patient or to the customer on aspects of cleanliness and the safest ideas whereby better health can be promoted^{2,3}.

Recently under the umbrella of JINNAH SINDH MEDICAL UNIVERSITY (Karachi, Pakistan), a new Faculty of Pharmaceutical Sciences has been established to award Professional Pharm. D. Degree for qualified pharmacist. The mission of the college is to provide holistic study with intellectual, spiritual, emotional, social, cultural and physical development. Students are encouraged to develop knowledge, values and skills which will enrich lives and prepare them to provide services to national and international communities. The main Objectives are:

To impart state-of-the art education to students, who shall become experts on medication so as to meet

Correspondence: Dr. Shafaque Mehboob, Department of Pharmacology, Jinnah Sindh Medical University, Rafiqi H.J Shaheed Road, Karachi 75510, Pakistan.

Email: shafaque.mehboob@hotmail.com

the needs of the end users in an active and useful manner, both within the country and abroad.

To disseminate knowledge and emphasize fundamental principles of pharmaceutical sciences.

To develop specific skills in experimental design and the analysis of experimental data.

To understand how medicines are synthesized, developed, manufactured and marketed.

To be able to supply medicines to patients in accordance with pharmaceutical knowledge, legislation and codes of professional conduct and practice.

To have an appreciation of the principles of quality assurance in all aspects of scientific and professional activities.

To have an appreciation of research methodologies relevant to natural clinical and pharmaceutical science.

To conduct graduate and post graduate education and research leading to higher degrees in pharmaceutics, pharmaceutical microbiology, pharmacology and pharmacognosy.

It is well understood that health education is not merely informing people about health matters. There is more to it. That is to motivate people to take whatever action they have been informed to do for sound health practice. It is a fact that now a days remedies once regarded with respect to the mysterious and the unknown are a part of our daily lives like other household articles. Health education must. Therefore, cover the proper use of medicines. Is there anyone better qualified by professional calling to perform this educational mission than a pharmacist?

Jinnah Sindh Medical University believes that the role of a pharmacist is to serve society as professional responsible for the appropriate use of medications to achieve optimal therapeutic outcomes.

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