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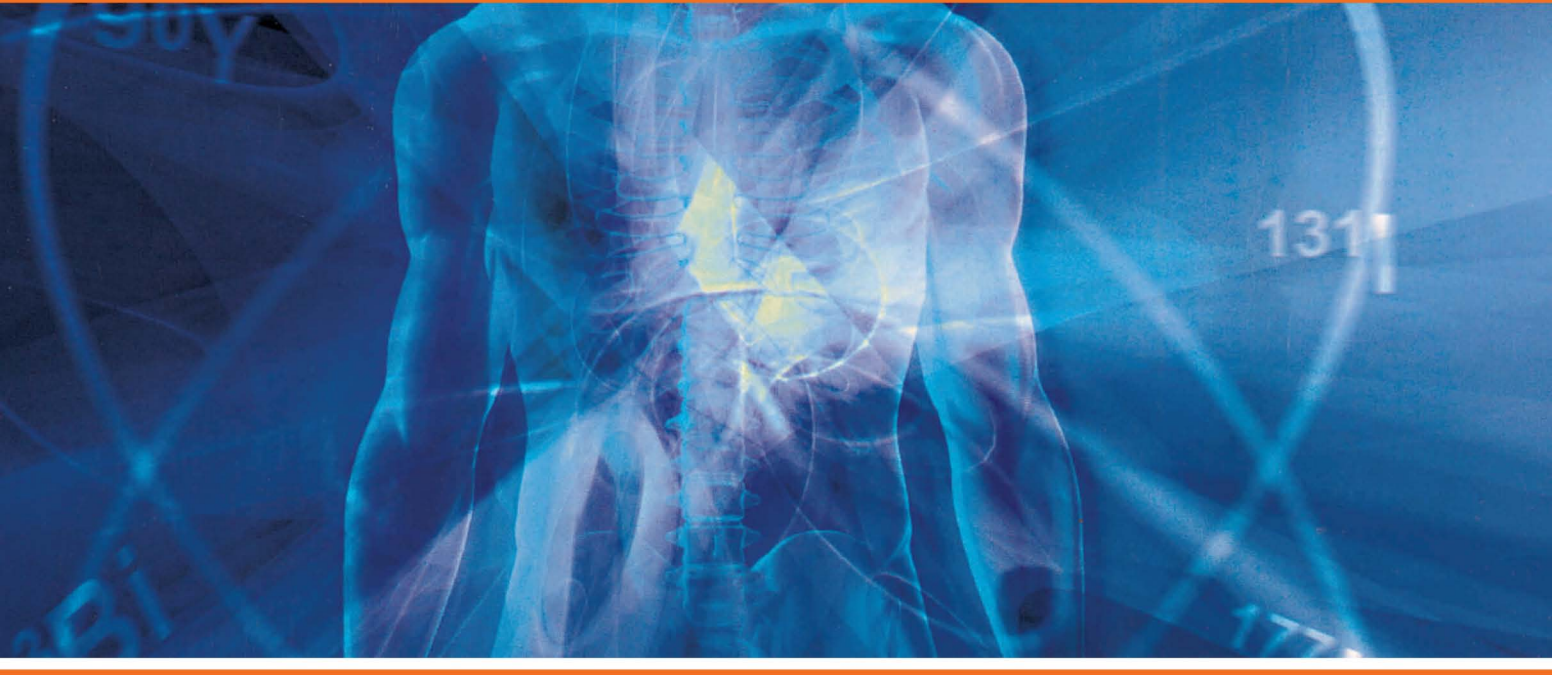

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EDITORIAL

Towards Competency Based Undergraduate Curriculum In Pakistan

Naeem A Jafarey

Knowledge in the biomedical field has grown exponentially, and is likely to keep on growing exponentially. Not only has the quantum of knowledge in the traditional subjects grown, but completely new subjects have been added in biomedical science. Thus, it is impossible for any one person to know everything about a subject. Hence,the need towards specialization has emerged in narrower and narrower sub-specialities. This situation has created a dilemma for those planning the undergraduate MBBS curriculum. Since it is impossible to know everything, teaching everything is also impossible.

The critical question is 'what should be included in the five year MBBS curriculum?'Or if we frame the same questiondifferently and ask'what should be excluded from the undergraduate curriculum?' Subject specialists of both basic and clinical sciences view the curriculum from their specialitypoint of view,and always tend to demand more time for their respective speciality. If the advices of subject specialists are taken then even five years of MBBS education are not sufficient to gain mastery over one of the undergraduate subjects, what to say about all of them.We need to remember that after graduation, the MBBS graduate will have innumerable options for specialization. So, what the MBBS should aim to cover in five years is which actually forms the 'core' that is applicable to all specialities.

One way of approaching this dilemma is to decide what is 'relevant'to the needs of the fresh graduate. In other words,'what should the fresh graduates be able to do?' Once we agree on that, then we can decide what factual knowledge, skills and attitudes an MBBS graduate needs to function as a physician with the desired competencies. This curricular concept is known as competency-based curriculum and its focus is preparing physicians for societal and patient needs[1-4]. Presently, students spend most time on memorizing innumerable facts which are likely tobecome outdated by the time they graduate, and thus graduates will find themselves inadequately prepared to practice in a fast changing clinical environment.

If 'relevance'is the key word in deciding what should be included in MBBS curriculum, then the competencies need to be discussed in a much wider forum, involving all the stakeholders, and not just the faculty of medical institutes. If we tend to rely only on subject specialists recommendations, the curriculum will be too focused on the individual specialist chosen field.Ultimately, the graduates are expected to manage the health services of the country, and therefore the managers of health services should beone of the key stakeholders to advise the curriculum planners on the desired competencies of an MBBS graduate.However, faculty engagement is central for the achievement of the desired competencies.

Our present subject-hospital based curriculum is what we in Pakistan inherited in 1947 from British India, which inturnwas based on the British curriculum model. The General Medical Council(GMC) has since then totally revised the rules and regulations of its undergraduate program, and now hasdefined the competencies that a graduate should acquire on completion of their medical studies. The GMC document 'Tomorrow's Doctors'[5]emphasizes among other attributes such as good clinical care,the scientific basis of practice,relationships with patients, working with colleagues and professional values. The GMC document does not mention subjects, number of hours or number of marks for each examining subject. Moreover, how the medical colleges train and assess students,for the desired competencies is left to the individual colleges. The main concern of GMC is thatthe graduates acquire the defined competencies,and are prepared to pursue their further training.

In Pakistan's context, the first step towards change to competency-based curriculum is to recognize that there is a need for change. Unless we address the status quo mindset which resists change, no progress can be made towards preparing medical undergraduates for societal needs. The subject-hospital based curriculum, the Flexnerian[6]curriculum modeldesigned a hundred years ago, was most appropriate to the needs of the first half of the twentieth century when there were just physicians andno specialists, and the tertiary care hospital did not exist for patient care. We now have to plan for the prevailing environment, and the present needs of Pakistan. Today's tertiary care hospitals equipped with high–tech equipment, and practicing specialists, subspecialists are best suited for training of postgraduates in different specialities. The role of tertiary care centers in undergraduate education has become marginal, and we need to explore other primary or secondary health facilities as well for medical students'training. Now is the time to rethink towardstraining undergraduates with competencies to serve patients and communities.

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ORIGINAL ARTICLE

Print And Electronic Media: Cause Of Depression

Shehnaz A Shaikh, Humayun Bin Irfan, Hira Ishtiaq, Ishaq Azeem Asghar, Madiha Haroon, Farida Ali Javed, Jawed Altaf Baig, Khursheed Hashmi

Abstract

Objective: To assess depression in normal people and associate it with print and electronic media of Pakistan.

Methodology: The study was descriptive, cross-sectional and conducted from July to November 2011. Three hundred and twenty men and women, with age range of 20-70 years were included in study following informed consent. A structured questionnaire with five items of Yes and No category relating media to depression was used. To assess the severity of depression Zung self –rating depression scale was used. Subjects with score of 80-90 were excluded as this score is of clinical depression. Data analysis was done by SPSS version 13.0. Pearson Chi-square was applied with $p<0.01$ considered statistically significant.

Results: Depression was seen in 55 % of subjects on reading newspaper. Watching television caused depression in 59.7% ($p<0001$). In 68% subjects daily routine life was disturbed ($p<0.01$). The highest rate of depression 32.6% was due to watching political news, while 28.3 % were by photographs and visuals of dead bodies and 24.6% by news of terrorism. Prevalence of mildly and moderately depressed individuals was 56.3 % and 15.8% respectively.

Conclusion: Reading newspaper and watching television causes depression. The content of news on media in particular leads to depression.

Key words: Media, depression, depression scale

Introduction

Depression is a state of low mood and aversion to activity. Depressed people suffer from common symptoms of mood disorders including feeling of sadness, irritable, restlessness and many lose interest in activities that once were pleasurable. In extreme cases of depression few even contemplate or attempt suicide[1]. Evidence suggests that psycho-social stress precedes the onset of depression[2]. In recent years prolonged exposure to media has been attributed as the leading cause of depression[3]

In Pakistan, mental health services have not kept pace at a satisfactory level as compared to other health related fields[4]. Also patients with symptoms of mental disorders avoid seeking professional help. One reason for this is that several myths are attached to these illnesses.

Media has a major impact on promoting a positive image of mental patients but somehow discussions on mental illnesses by non-professionals on the media has lead to deception and distortion creating abhorrence about patients with mental disorders [4]. The influx of TV channels accessible to person at all ages and brackets with sometimes un-ethical and un-authentic opinions need urgent attention[4]. Media exposures have been linked to the presence of psychiatric conditions, but few studies have investigated the association between media exposure and depression[3, 5]. Television exposure and total media exposure in adolescence are associated with increase odds of depressive symptoms in young adulthood, especially in young men.[3]

There are several possible ways by which media exposure enhance the risk of depression, the long time spent in watching Television could be used in socializing, or participating in sports whether indoor or outdoor or engaging in intellectual activities – all of which may protect against depression.[6] Watching TV at night may disrupt sleep, which is important for normal brain and emotional development[7]. Message transmitted through the media may reinforce aggression and other risky behaviors interfere with identity development or inspire fear and anxiety[6, 7] Depression is the most common psychiatric illness in the world, affecting 15 percent of all people at some point in their lives. Although about 70 percent of the depressed patients respond to treatment, three-fourth will experience a recurrence of their illness within 10 years, in addition an estimated 60 percent of the depressed people remain undiagnosed and untreated [8]

Symptoms of depression are assessed by various methods; such as depression rating- scales compiled by renowned psychiatrists but have to be administered by trained and professional observers.

The present study utilized Zung self-rating scale of depression to assess the severity of depression [9] if depression is present in apparently normal individuals and relate depression with print and electronic media.

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The response of Pakistan's electronic media to disturbing news of violence, disasters within and outside Pakistan has led to increase number of hours of public exposure to television. We decided to undertake a study on determining the effect of media on the minds of Pakistani population.

Material and Methods:

This descriptive and cross sectional study was conducted from July to November 2011 at Liaquat National Hospital and Medical College. The study subjects were randomly selected from the general population. Informed consent was obtained. Three hundred and twenty apparently healthy subjects (52.5 % male and 47.8% females) with age ranging from 20-70 years, having no physical illness, were included in the study. A structured questionnaire especially designed and tested for the study was administered. The questionnaire included five items of Yes and No category on use of media and media effects on depression. Zung self-rating scale was used for assessing severity of depression among men and women.[10] Subjects with score of 80-90 were excluded from the study as this defines clinical depression and patients with diagnosed depression are presented with psychological and somatic symptoms[11]

Statistical analysis:

Data analysis was done by using SPSS version 13.0. Pearson Chi-square test was applied to observe rate of depression with different parameters. The value of $P<0.01$ was considered statistically significant.

RESULT:

In 320 apparently healthy subjects included in the study, 52.5 % were males and 47.8% females. Response of subjects on use of print and electronic media is given in (Table 1) which shows that 84.4% read newspaper daily, 55.3% read English newspaper, while 33.4% read national language Urdu newspaper. In our study group 93.8% watched Television regularly. Responding to specific television programs, 19.4% watched sports program, 31.3% television dramas, 25.6% movies, 15.0% news, 6.6% current affairs and 2.2% religious programs. On reaction to watching depressing news, 68.8% switched to entertainment channels, 20% switched to other news channels and 11.2% switched off TV. There were 40.6% people feeling depressed by watching Talk Shows. Fifty five percent people said that reading newspaper caused depressed feeling, while 45% were indifferent, they did not feel depressed. The difference on Pearson Chi-square was significant $p<0.001$ (Table II). Sixty eight percent indicated that depression was causing disturbance in their daily routine life while 32% were not affected ($p<0.01$) (Table II). Table III shows prevalence of depression amongst subjects which gave results as mildly depressed, 56.3 %, moderately and severely depressed 5.8 % and 1.6 % respectively while 26.3 % were not at all depressed. Table IV shows various types of news causing depression; natural disaster has 8.2 %, news of terrorism 24.6%, social news 6.3 %, photos and visuals of dead bodies 28.3 % and political news 32.6 %

Table I: Response of subjects on use of Print and Electronic media

Question	Yes % n= 320	No % n= 320
Do you read newspaper?	84.4	15.6
Which newspaper do you read? a) English b) Urdu c) Sindhi d) Misc.	 55.3 33.4 2.8 1.9	NA
Do you watch TV?	93.8	6.2
What type of programs do you usually watch? a) Sports b) Drama c) Movies d) News e) Current affairs f) Religious	 19.4 31.3 25.6 15.0 6.6 2.2	NA
What is your reaction after watching depressing news? a) Switch off TV b) Switch to other entertainment channels c) Switch to other News channels	 11.2 68.8 20.0	NA
Do you get depressed after watching talk shows?	40.6	59.4

Table II: Effect of Media on depression

Question	Yes %	No %	P – value
Do you get depressed after reading newspaper?	55	45	P<0.001
Do you get depressed after watching TV News?	59.7	40.3	P<0.001
Do you think this depression is affecting your daily routine?	67.5	32.5	P<0.01

Table III: Prevalence of depression:

n=320	%
No depression	26.3%
Mild depression	56.3%
Moderate depression	15.8%
Severe depression	1.6%

Table IV: Types of news causing depression

Types of news	%
Natural disaster	8.2 %
News of terrorism	24.6 %
Social news	6.3 %
Photos and visuals of dead bodies	28.3 %
Political news	32.6 %

Discussion:

Depression is a figurative and literal killer[12]. Biochemically depression is associated with a decrease in brain –derived neurotrophic factor (BDNF), which was the second factor to be identified after Nerve Growth Factor (NGF) [13]. BDNF in the brain is active in hippocampus, cortex, and basal forebrain- areas vital to learning, memory and higher thinking.[13] BDNF itself is important for long –term memory[13].There is also an increase in oxidative stress, glucocorticoids and inflammatory cytokines[14]. An increase of glucocorticoids decreases the expression of BDNF, which eventually leads to atrophy of hippocampus, and other limbic structures[14, 15]. Thus an etiological link exists between depression and BDNF [15].

Media exposure has since long been linked with depression. World Health Organization (WHO), reports that the relationship between media exposure and depression is the leading cause of morbidity worldwide and is very common in adolescence[16]. In developing countries like Pakistan, 1% of the population suffers from severe and 10 % from mild mental disorders [17]

The present study observed that of 320 participants, 93.8% watched television. Moreover, depression caused by television exposure is not gender specific as 52.5% males and 47.8% females were affected (Table I). In previous study, an excessive exposure to TV in teens has been linked to an increased risk for depression in early adulthood[18]

Electronic media not alone is a cause of depression, the print media content as well has contributed to depression.

Recently, in Pakistan, several new newspapers have emerged in English, national and regional languages. Similarly, the influx of private television channels has been a leading factor in shaping population opinions on political, social events and changes in values and behaviors.

However, the content of both print and electronic media has raised concerns in general public. In view of Pakistan's security concerns, several incidents of violence including terrorist attacks have dominated both print and electronic media. Social activists, parents, psychologists and psychiatrists have severely criticized news channels for repeatedly reporting news of violence and criminal activities along with portraying images of blood, and dead bodies[19]. This study confirms that people get disturbed on watching news and 68.8% switch to other entertainment channels, 20% to other news channels while only 11.2% switch off the television.

The present study confirms that amongst print media about 84.4% read newspaper everyday (Table I). A high rate of depression was found among those who read newspaper and the result was significant (p<0.001, Table II). Findings of another study on teens exposed to long hours of watching TV reported that teenagers are at high risks for depression as do adults[19]. Our study subjects had age range 20-70 years both teenagers and adults, and the result is in agreement with the previous study on watching TV and feeling of depression [16,18] (p<0.001, Table II). The depression caused by TV watching was affecting daily routine life and was significant (p<0.001, Table II).

Dr Primack's theory on relating media with depression has categorically identified several bad news, depressing events shown on TV and repeated exposures

as the root cause of depression that lead to internalization in viewers[3].

The present study reported 28.3% were depressed on watching photographs and visuals of dead bodies, while 32.6% felt depressed on watching political news. (Table IV) These findings are in agreement with Dr Primack's theory. The high rate of depression on hearing political news is a major problem relevant to the context of Pakistan.

According to Human Right Commission of Pakistan (HRCP) report 34% of the country's population suffered from some form of mental illness[4]. The Mental Health Ordinance of Pakistan promulgated on 20th February 2001, has yet to be implemented.[4]

In a national longitudinal survey of adolescent health, investigators looked at the relationship between electronic media and exposure in 4142 adolescents who were not depressed at baseline, but subsequently developed depression on 7-year follow up study of 4142 adolescents, 308 (7.4%) reported symptoms consistent with depression, and researcher found these individuals had watched more television than non-depressed individuals at baseline, 2.64 hours against 2.28 hours per day. This association was statistically significant[3]

A study correlated the duration of watching TV with depression and found that people who watched TV less than three hours a day were less depressed than those who watched more than nine hours a day[19]. Study on youth and media use on an average of 7 hours per day reported that using media (TV, computer, internet, video games, and cell phones) had a negative effect on its user[2]. Prolonged hours of television and computer related exposure facilitate individual activities rather than sharing common social interests and activities[20, 21]. The limitation of this study is that it focused on news and related activities.

Based on Zung scale of depression our results indicated that the prevalence of depression among the subjects was mild in 56.3%, moderate 15.6% and severely depressed 1.6% (Table III).

Conclusion:

Media particularly the content of both print and electronic has relationship with depression. This study reveals that reading of newspaper and watching TV News cause depression.

Recommendations:

Concentrated actions are required from all stakeholders including parents, educational institutions to encourage youth to develop interest in outdoor activities such as sports, educational trips, library visits, and social activities. Even adults need to engage in activities that will restrain them from unnecessarily exposure to prolonged hours of television news that lead to depression. Further large cross sectional studies are needed to find out the correlation of media with depression.

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ORIGINAL ARTICLE

Correlation Of Hematocrit And Hemoglobin With Obesity, Serum Lipids And Aldosterone In Newly Diagnosed Hypertensive Patients

Sadiqa Syed, Shazia Shakoor, Masood A Qureshi

Abstract

Objective: To determine the relationship of obesity indicators with certain hemodynamic and metabolic cardiovascular risk factors, at the initial diagnosis of hypertension in a random population, in search of a treatable cause

Methods: A case control study was conducted on 201 subjects aged between 25-60 years, diagnosed primarily as prehypertensive or hypertensive stage I and II , selected from five general practitioners clinics in Karachi. Estimated of hematocrit, hemoglobin, triglycerides, low density lipoproteins, serum potassium level and aldosterone was done. Their body mass index and waist hip ratio were calculated by measuring body weight, height, waist and hip circumference. The values obtained were compared with 75 controls with normal blood pressure.

The mean and standard deviation were computed. Analysis was done by SPSS version 15.LSD test was applied to compare pair-wise group. Pearson's correlation was applied to find out association of different variables with one another, within each of the four groups

Results: The overall percentages of overweight and obese subjects were higher in all four groups. The mean hematocrit and hemoglobin levels were highest in HTN stage –I (44.7±5.25 and15.4±2.20 respectively). Hemoglobin was strongly correlated to systolic blood pressure and waist hip ratio in both hypertension stages-I and II ($p<0.01$). Whereas hematocrit was positively correlated to body mass index, triglycerides, serum potassium and aldosterone levels in both stages of hypertension ($p<0.01$)

Conclusion: High hematocrit, hemoglobin, triglyceride levels, visceral fat accumulation and aldosterone secretion are important and independent risk factors for hypertension.

Key words: hypertension, hematocrit, hemoglobin, triglyceride, aldosterone

Introduction

Hematocrit (Hct) or packed cell volume represents the cellular portion of blood mainly red blood cells, expressed as percentage (% vol/vol) and is the major determinant of whole blood viscosity (WBV). [1] Other factors that contribute to blood viscosity in addition to Hct include plasma proteins, plasma lipids and other rheological factors. [2] It has long been known after Poiseuille-Hagen equation, that a strong association exists between WBV and hypertension (HTN), as hyperviscosity affects peripheral resistance (PR), and thus blood pressure (BP), not only by increasing resistance to flow and workload on heart, but also by hindering vasodilation. [3]

Hct above the normal range along with related hematological variables such as hemoglobin (Hb), red blood cell count and mean corpuscular volume, predispose to both arterial and venous thrombosis, in primary and secondary erythropoiesis [4] and may be a responsible factor in causing cerebral ischemia, especially if associated with inflammation.[5] Hb the oxygen carrying pigment in the blood, is an important nitric oxide (NO) buffer and a modulator of its bioavailability and hence plays a central role in vascular function.

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Population-based studies have consistently demonstrated that on average Hb is raised in patients with essential HTN; thus it is suggested that Hb-dependent mechanism contributes to endothelial dysfunction in HTN by influencing availability of NO. [6] Hb, by a series of biochemical processes including NO oxidation and nitrosylation of iron molecules and sulfur containing amino acids in globin molecules, neutralizes the NO very effectively. This direct negative effect on NO availability might explain the link between high Hct and cardiovascular disease (CVD).[7] A study revealed that Hb level > 17 g/dL is associated with coronary artery disease (CAD). [8]

Several epidemiological studies supported the evidence that elevated blood viscosity and Hb concentration are related to HTN, insulin resistance (IR) [9], metabolic syndrome, severe obesity and peripheral atherosclerosis in adults [10]. A study showed that low density lipoprotein cholesterol (LDL) is the principal lipid that independently influences the WBV [11], whereas other studies suggested that high triglyceride (TG) and low HDL levels are responsible for elevating WBV and promoting atherosclerosis. [12, 13] WBV is inversely related to flow and may predispose to IR and type 2 diabetes mellitus, by limiting delivery of glucose, insulin and oxygen to metabolically active tissues [14]

Prospective studies have revealed that intraperitoneal and posterior subcutaneous fat mass is strongly linked with dyslipidemia and IR [15]. Moreover free fatty acids released from visceral adipose tissues have been shown to increase IR and aldosterone production.[16] Plasma renin and aldosterone levels both, have been reported to be three folds greater with secondary erythrocytosis compared to controls. [17]

Epidemiologists and biologists have been trying to identify new risk factors, particularly modifiable risk factors that could explain some of the variability in HTN

and CVD, not explained by traditional risk factors. Thus over hundred risk factors have been proposed by Framingham Heart Study. This study focuses on finding an association and correlation between hemodynamic factors Hct and Hb, plasma lipids concentration (TG, LDL), body fat composition, reflected by Body mass index (BMI), Waist hip ratio (WHR) and aldosterone hormone.

Subjects and Methods

It was a case control study with purposive sampling, carried out on 276 subjects, aged between 25-60 years, selected from five general practitioners clinics in Karachi and were categorized into four groups according to 7th JNC report. [18] The control group (A) had normal systolic (SBP) and Diastolic BP (DBP). The prehypertension (pre-HTN) group (B) had systolic BP between 120-140 mmHg and diastolic BP >80 and < 90 mmHg, hypertension stage-I (C) with SBP >140 and <160 mmHg; DBP >90 and <100 mmHg and Stage-II (D) with SBP >160 and DBP >100 mmHg.

Patients suffering from any other disease (cardiac, renal, hepatic etc) other than HTN were excluded from study (exclusion criteria).

BP measurement: both systolic and diastolic BP were measured twice by mercury sphygmomanometer half an hour apart and then averaged.

Anthropometric measurements: height and weight were measured and BMI and WHR were calculated by formulae. BMI= Weight in Kg/ height in cm^2 WHR= waist in cm/height in cm

Measurement of Hematocrit: traditionally it is determined by measuring the height of red cell column in microhematocrit tube following centrifugation. Automated analyzer (Advia) calculates the Hct by multiplying the red cell count and the mean red cell volume, both of which are measured directly by machine. Normal value: 38-42%

Estimation of hemoglobin: is done traditionally using the cyanomethemoglobin method. To measure the Hb concentration, a lysing agent is added to a sample of diluted blood, which disrupts all red cells in the sample and released Hb, which is then converted into Cyanomethemoglobin and the concentration is read by spectrophotometer with the wavelength set at peak absorbance of cyanomethemoglobin. The concentration of Hb is then calculated from the optical density of the solution. Hb concentration is 1/3rd of Hct and is reported as grams/dL of blood. Normal values: 12-15 g/dL

Quantitative Determinations of TG and LDL were performed by enzymatic in vitro test in human serum on Roche cilinical chemistry analyzer using commercially avaialbale GPO-PAP and LDL kit respectively

Values NCEP[19]	**TG mg/dL**	**LDL mg/dL**
Normal	<150	<100
Borderline:	>150-199	130-159
High:	>200-499	> 160

Measurement of Aldosterone: was done by ^{125}I radioimmunoassay, based on aldosterone specific antibody immobilized to the wall of polypropylene tube (ELISA)

Normal value: Standing: 4-31 ng/dL, Recumbent: 1-16 ng/dL

Ethical consideration: Written consents of subjects were taken and study was approved by Board of advanced studies of Karachi University.

Results

The mean Hct level of HTN stage-I was significantly higher ($p<0.05$) than the mean of HTN stage-II (44.7±5.25 vs 42.0±3.83; $p=0.014$) as well as control and pre-HTN groups, as shown in Table 1. Hct level showed significant positive correlations with BMI, TG, K+ and aldosterone, in both stages-I and II of HTN (Table 2)

The mean Hb value was significantly higher in HTN stage-I (15.4±2.20) as compared to control, pre-HTN group ($p<0.001$), and HTN stage-II group i.e. 13.2±1.56 ($p<0.005$) as shown in Table 3. Significant correlation was seen between Hb level and systolic BP only in HTN stage-I, whereas no positive relation was observed with diastolic BP. Hb was positively correlated to systolic BP and WHR in both HTN stages -I and II (Table 2).

The serum TG level was on higher side in HTN stage-I (161.8±79.9) and II (166.6±66.7) as compared to control and pre-HTN groups. The mean LDL level was 106.5±30.7, 105.6±32.7, 116.4±32.9, and 103.7±29.2 in four groups respectively, the highest level being in HTN stage-I (Table 4).

The values of serum K+ were insignificant among four groups: 4.5±0.43, 4.47±0.42, 4.26±0.51 and 4.41±0.45 respectively. The mean aldosterone level was on higher normal side in HTN stages-I and II, i.e. 12.41±5.72, and 2.05±6.84 (Table 4).

Statistical analysis: Data was analyzed by SPSS version 15. The variables were presented as Mean ± standard deviation. Analysis of variance was performed to compare four study groups and LSD test was applied to compare pair-wise group.

Test of linear correlation was applied to asses relationship of different variable with systolic and diastolic pressure. Coefficient correlations of parameters were carried out with each other and within each of the four groups to identify the association of different variables with one another in different stages of hypertension. P value is taken as significant at <0.05.

Discussion

One of the objectives of evaluation of patients with documented HTN is to reveal identifiable causes of high BP.

The purpose of this study was to explore the association of some of the environmental and endogenous risk factors and to identify their correlation in different stages of HTN in Pakistani population, whose 18% adults suffer from this disease.[20] The BP level attributed to HTN in most of the studies done in Pakistan was >140/90 mmHg, but in this study subjects were classified into three groups

of HTN including the pre-HTN stage with high normal BP.

Table 1: Comparison of mean Hematocrit (Hct) among study groups (n=276)

S #	A	B	C	D
Group	Control (n = 75)	Pre HTN (n = 55)	HTN stage-I (n = 70)	HTN stage-II (n = 76)
Mean± SD	40.3 ± 4.30	40.4 ± 3.50	44.7 ± 5.25	42.0 ± 3.83
Pair-wise comparison statistical significance	-	v/s A=0.929	v/s A=0.001*	v/s A=0.381
	-	v/s C=0.003*	v/s D=0.014*	-
	-	v/s D=0.474	-	-

* The mean difference is significant at the 0.05 level.

Table 2: Coefficient correlation of HCT and Hb with other variables in HTN stage-I and II

Variable	SBP	BMI	WHR	TG	Serum K+	Aldosterone
Hemoglobin						
HTN stage-I	.396**	.077	.246**	.012	.116	.134
HTN Stage-II	.450**	.072	.236**	.073	.171	.052
Hematocrit						
HTN stage-I	.097	.298**	.220	.362**	.266*	.615**
HTN stage-II	.082	.263**	.247*	.340**	.294**	.533**

** Significant at the 0.01 level (2-tailed)
* Significant at the 0.05 level (2-tailed)

Table 3: Comparison of mean Hemoglobin (Hb) among study groups (n = 276)

S #	A	B	C	D
Group	Control (n = 75)	Pre HTN (n = 55)	HTN stage-I (n = 70)	HTN stage-II (n = 76)
Mean± SD	12.3 ± 1.84	12.7 ± 1.97	15.4 ± 2.20	13.2 ± 1.56
Pair-wise comparison statistical significance	-	v/s A=0.352	v/s A<0.001*	v/s A=0.004*
	-	v/s C<0.001*	v/s D=0.024*	-
	-	v/s D=0.08	-	-

* The mean difference is significant at the 0.05 level.

Table 4: comparison of mean of different variables among study groups (Mean±SD)

Group	Control	Pre-HTN	HTN Stage-I	HTN stage-II
BMI	24.9±3.77	26.4±4.47	28.4±4.53*	26.6±5.33
WHR	0.90±0.06	0.94±0.07	0.99±0.05*	0.99±0.06
TG	134.6±60.3	136.1±62.2	161.8±79.9*	166.6±66.7
LDL	106.5±30.7	105.6±32.7	116.4±32.9*	103.7±29.2*
Serum K+	4.5±0.43	4.47±0.42	4.26±0.51	4.41±0.45
Aldosterone	9.17±3.49	8.76±3.31	12.41±5.72*	12.05±6.85

* The mean difference is significant at 0.05 level

Most of the participants were educated and belonged to lower middle class; detail of subject profile has been published previously. [21]

Hct and HTN are intricately correlated, such that lowering the Hct can directly decrease BP by altering total peripheral resistance. Blood viscosity can therefore be employed as a very useful and sensitive indicator of BP. [22] The mean Hct level of HTN stage-I was significantly higher than the mean of all other groups; whereas the mean Hb level was also significantly higher in HTN stage-I (15.4±2.2) as compared to control and pre-HTN groups ($p<0.001$) and HTN stage-II group ($p<0.05$). Significant correlation was seen between Hb level and systolic BP both in HTN stage-I and II.

The quantity and distribution of body fat was assessed by two indicators, BMI and WHR in this study, as WHR is regarded as three times better predictor of risk of heart attack as compared to BMI.[23] This study confirmed that percentage of overweight and obese persons, has risen sharply in Pakistani general population even in middle and lower classes. In this study 69 % subjects in control group, 80% in pre-HTN, 90% in stage-I and 76 % in stage-II were overweight and obese, which is contrary to previously reported data showing 25% overweight and 10.3% obese people in our population. [24]

Both Hct and Hb were positively correlated to BMI in HTN stage-II, and to WHR in HTN stage-I and II. This suggests a link between these hematologic parameters and obesity, as strongly claimed by a latest study that among classical cardiovascular risk factors, WHR is closely related to blood viscosity. [25] Another study supported our finding in which untreated hypertensive patients had higher BMI, Hct and BP in both sexes. [26] A study on Iranian women reported that obese women have greater iron stores in terms of serum ferritin, Hb and Hct concentration than do non-obese women and are more prone to develop HTN. [27]

A correlation between Hb and IR was found in non-smokers in a study which also showed association of Hb with other components of IR such as BMI, WHR, lipid profiles, and systolic BP, which is consistent with our findings.[28] Our results thus provide support for a relationship between IR and hematological parameters such as Hb and Hct. Previously a study revealed that high erythrocyte count and Hb are associated with obesity and HTN [9] and another study documented that with treatment of anemia, increased Hct was followed by increased blood viscosity together with a rise of BP. [29]

Hyperviscosity has been found to be related to not only HTN but also IR, metabolic syndrome, severe obesity and peripheral atherosclerosis in adults.[10] The importance of TG as an independent risk factor has been reported by several studies, as TG rich lipoproteins penetrate endothelial cell layer, forming foal cells, a hallmark of atherosclerosis, the process especially enhanced in low shear stress areas of arteries.[30] IR and hyperinsulinemia have been observed in over 70% of non-obese, non-diabetic subjects with essential HTN, suggesting the resistance results from endothelial dysfunction and impaired endothelial dependent vasodilation.[31] A study confirmed that insulin was related to BMI and aldosterone in both normotensive and hypertensive subjects. [32] This study reported significant correlation of Hct with hormone aldosterone in both HTN stage-I and II for the first time.

The interrelationship among these factors as evident by this study, may tentatively suggest the possible sequence of mechanisms causing HTN as: visceral fat accumulation (TG, LDL) in upper abdomen impairs endothelial function, leading to a decrease in responsiveness of cells to insulin (IR) as well as decrease K+ entry into the cells, increasing plasma K+ level, which is a very strong stimulus for secretion of aldosterone, and needs to increase only 1 meq/L to stimulate its release from adrenal cortex. The aldosterone in turn, causes sodium and water retention. High Hct further aggravates the condition by increasing peripheral resistance and Hb impairs vasodilation by affecting NO availability; thus all these factors cumulatively result in HTN

Conclusion

Patients with a new diagnosis of HTN should be evaluated with a history, physical examination and the initial workup which should include the simple and cost effective tests, that provide an insight to the possible treatable causes of high BP and assessment for the presence of target organ damage. To promote primary prevention of HTN, identification and monitoring of increase in weight, lipid profile, blood glucose level and other related factors in HTN-prone subjects are considered important to prevent Clustering of different risk factors.

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ORIGINAL ARTICLE

Comparison Of Vitamin B12 Level Among Vegetarian And Non Vegetarian Apparently Healthy Individuals In District Tharparkar

Aneel Kapoor, Nudrat Anwar Zuberi, Muktiar Baig

ABSTRACT

Objective: Subjects adopting a vegetarian diet are liable to vitamin B12 deficiency. The current work was undertaken to investigate vitamin B12 status in apparently healthy vegetarians in Mithi, district Tharparkar, Sindh.

Subjects and methods: This cross sectional study was conducted in the department of Biochemistry, BMSI, JPMC Karachi and blood samples were collected from Mithi district Tharparkar, Sindh, during the period of Febuary 2012 to June 2012. One hundred vegetarian (74 males and 26 females) and one hundred non- vegetarians (72 males and 28 females), age ranging from 20-40 years were enrolled for this study. Hemogloblin concentration, means corpuscular volume and serum vitamin B12 levels were measured, using conventional methods.

Results: Mean serum vitamin B12 level and mean hemoglobin concentration were significantly lower ($p<0.001$) while mean corpuscular volume (MCV) was significantly higher ($p<0.001$) in vegetarian as compared to non-vegetarian. In vegetarian group 51(51%) subjects had vitamin B12 level less than cut off value (200 pg/ml), in this group, 38 out of 74 (51.3%) and 13 out of 26 (50%) were males and females respectively. In non vegetarian group 21(21%) subjects had vitamin B12 deficiency and 09 out of 72 (12.5%) and 12 out of 28(43%) were males and females respectively.

Conclusion: Vegetarians seems to be more prone to develop vitamin B12 deficiency so they should take vitamin B12 supplement and/or B-12 fortified products to avoid its deficiency consequences.

Key Words: Vitamin B12**,** Vegetarian, non-vegetarian.

INTRODUCTION

Vitamin B12 is known to be predominantly present in animal tissue and generally absent in plants, with the exception of some seaweeds[1-2]. Therefore, vegetarians who consume less animal source food are considered a risk group for vitamin B12 deficiency; although vitamin B12 is seldom exhausted due to the enterohepatic circulation, and the clinical manifestation of vitamin B12 deficiency rarely occurs, even without intake of vitamin B12 for many years[2]. However, it is also well known that eliminating all animal products from the diet increases the risk of certain nutritional deficiencies. Micronutrients of special concern for the vegetarians include vitamin B12 and D, calcium, long-chain n-3 fatty acids and Zinc[3-4]. Vitamin B12 is an essential micronutrient that plays essential role in cell division, in one-carbon metabolism[5], DNA synthesis, *erythropoiesis* and neurologic function[6].

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Severe clinical symptoms of B12 deficiency which include ataxia, psychoses, paresthesia, disorientation, dementia, mood or motor disturbances, may appear with or without obviously known hematological symptoms (megaloblastic anemia, macrocytosis)[7]. It has been reported that vitamin B12 deficiency is associated with coronary artery disease in Indian population[8].

The morphological characteristic of folate or vitamin B12 deficiency anemia is generally macrocytic due to immature erythrocytes resulting from defective DNA synthesis[9].

Vegetarians who avoid all animal products including milk and its products are referred to as vegans[10]. Vegetarian are at greater risk of vitamin B12 deficiency than are non-vegetarians because most of the sources of vitamin are meat, fish and eggs. Few studies in Indian have reported high prevalence of vitamin B12 deficiency in vegetarians[11-12].

This study was carried out in the population of Mithi, district Tharparkar (Sindh) where a significant proportion of individuals (Hindu community) adhere to a vegetarian diet throughout their lifespan and have never consumed animal products except in the form of milk or milk products due to family conventions or religious doctrines. Thus, this is an ideal population to find out vitamin B12 deficiency, which is only sourced from animal products.

The objective of present study was to compare vitamin B12 level among vegetarian and non vegetarian apparently healthy individuals in district Tharparkar, Sindh

SUBJECTS AND METHODS

This study was conducted in the department of Biochemistry BMSI , JPMC Karachi from Febuary 2012 to June 2012. A total of 200 healthy volunteers, age ranging from 20-40 years were recruited for this study, from the general population of Mithi district Tharparkar, Sindh. Out of 200 subjects, 100 were vegetarian (74 males and 26 females) and 100 non-vegetarians (72 males and 28 females). The vegetarian group had adhered to a vegetarian diet since their childhood and they do not eat beef, poultry, fish, shellfish or animal flesh of any kind, but do eat eggs and dairy products (lacto-ovo-vegetarians). The non-vegetarians were the omnivore taking food from all sources. The participants included were those who were apparently healthy, and had no physician-diagnosed disease (especially inflammatory disease). A detailed questionnaire with all the clinical data was completed for each participant on the day of recruitment. This included information about the participant's blood pressure, smoking habits, height and weight measurements, dietary status, milk consumption, etc. Individuals with following status were excluded from this study, those taking multi vitamins, diabetics, pregnant and lactating females, alcohol users, having gastrointestinal, autoimmune and chronic diseaseses.

Sample Collection

Five milliliter blood was collected from each volunteer, after an overnight fasting and haematological workup, including haemoglobin (Hb) and means corpuscular volume (MCV) was done on all the subjects using standard hematological and biochemical techniques. The serum was separated and stored at -70 ^{0}C until analyzed for vitamin B12. Hb and MCV were determined by coulter counter (Sysmex KX-21,Kobe Japan 2009) and vitamin B12 level was measured by the chemiluminescence enzyme immunoassay method by using immulite 1000 (USA 2010).The normal range of vitamin B12 levels was 200 to 900 pg/ml. The biochemically vitamin B12 deficiency was considered at a level below <200 pg/ml in study subjects[13-14].

All analyses were performed on SPSS version 16 .Values of quantitative variable were presented by mean with standard deviation and significance was estimated by Student's t- test.

Results

Table 1 shows that among vegetarian group the vitamin B12 level was significantly lower as compared to non vegetarians ($p<0.001$) The mean Hb level was significantly lower ($p<0.001$) while MCV was significantly higher ($p<0.001$) in vegetarian as compared to non vegetarian groups. Table 2 shows in vegetarian group 51(51%) subjects had vitamin B12 level less than cut off value (200 pg/ml). In vitamin B12 deficient group, 38 out of 74 (51.3%) and 13 out of 26(50%) were males and females respectively and no significant difference in mean value was observed between the two vitamin B12 deficient groups. In non vegetarian group 21(21%) subjects have had vitamin B12 level less than cut off value (200 pg/ml). In this group, 09 out of 72 (12.5%) and 12 out of 28(43%) were men and women respectively and no significant difference in mean value was observed between the two vitamin B12 deficient groups (mean values are not shown in the table).

Table 1 Comparison of serum B12, MCV and Hb vales in vegetarian and non-vegetarian

	Non- vegetarian	Vegetarian	P-Value
Vitamin B12	377.71± 87.28 pg/ml	214.82± 41.12 pg/ml*	0.001
MCV	88.8± 6.97fL	99.4± 4.9 fL*	0.001
HB	13.46± 1.82 g/dL	11.21± 1.7 g/dL*	0.001

Results are shown as Mean ± SD

P<0.05 was considered significant

Table 2 Serum vitamin B12 levels in vegetarian and non-vegetarian subjects according to gender

n= number of subjects

Variables	**Total number**	**B12 deficient (<200pg/ml)**		**B12 non-deficient (>200pg/ml)**	
		Vegetarian n (%)	**Non-vegetarian** n (%)	**Vegetarian** n (%)	**Non-vegetarian** n (%)
Male	146	38(51.3)	09(12.5)	36(48.6)	63(87.5)
Female	54	13(50)	12(42.9)	13(50)	16(57.1)
Total	200	51 (51)	21(21)	49(49)	79(79)

DISCUSSION

Deficiency of vitamin B12 is common because of inadequate dietary intake and/or malabsorption[14]. The deficiency state has a very wide presentation and can cause or exacerbate neuropsychiatric and other vague symptoms. It had been observed that vitamin B12 deficiency is far more prevalent than expected and majority of the cases remain undiagnosed. Therefore, early recognition of vitamin B12 deficiency becomes crucial for preventing irreversible damage[14].

The present study found that among vegetarian group the mean value of vitamin B12 level was significantly lower as compared to non vegetarians. Our results had concurred with other studies[5,12,15-16,]. Our results are not in agreement with few studies suggesting that serum vitamin B12 concentrations are not significantly lower in vegetarians compared to omnivores[17-19].

Kumar et al. [8] found that vegetarians have significantly lower vitamin B12 concentration and almost 50% of the vegetarians in their study population were lacto-vegetarians (individuals who consumed milk).

Our results showed that the mean Hb was significantly lower while MCV was significantly higher in vegetarian as compared to non vegetarian. Change in MCV has accounted by vitamin B12 status. Similar results were found by Obeid et al. [20].

A study by Reddy and Sanders[15] observed that Hb, MCV, MCH concentrations were significantly lower in the Indian vegetarians. It could be explained that if iron deficiency leading to microcytosis co-exists with megaloblastosis, macrocytosis may be masked and MCV may not be increased[21]. This may explain the macrocytosis in the present study in vitamin B12 deficiency.

Present results are consistent with the study by Reddy and Sanders [15] that observed markedly lower serum vitamin B12, higher MCV, MCH and lower erythrocyte (RBC) counts in Caucasian vegetarians compared with the Caucasian omnivores.

Our study had been focused on age group ranging 20-40 years, the reason was to limit the effects of increasing age on the vitamin B12 levels. The vitamin B12 deficiency had found 51% in vegetarians and 21% in non vegeerians. These results are consistent with those of Barghouti *et al.* [22] and Arora et al,[14] who found that the frequency of vitamin B12 deficiency in the same age group as 42.7% and 35% respectively. These results pointed out that the age seem to offer no substantial risk for developing B12 deficiency. This could be attributed to dietary limitations due to vegetarian dietary habits and lower socio economic status.

Arora et al. [14] have pointed out in their study that vegetarian diet is a considerable risk of developing vitamin B12 deficiency. In our vegetarian group 51% subjects were suffering from vitamin B12. These results are inconsistent with several studies[12,14,23-24]. Gupta *et al*, [24] found 47% of the Asian Indians had B12 deficiency confirming the high prevalence of this extent in Indians, though this study had been carried out on south Indians residing in Canada. This prevalence was quite similar to other studies carried out in India and with our study which carried out in Pakistan. This indicates that there are some other factors beyond vegetarian diet that could possibly be responsible for vitamin B12 deficiency.

vegetarians. These results are consistent with those of Barghouti.

In present study, in vegetarian group 51% males and 50% females and in non-vegetarian group 12% males and 43% females were suffering from vitamin B12 deficiency. We observed no significant gender-wise difference in prevalence of vitamin B12 deficiency in vegetarian group. This is in contrast to a study which pointed out that females are more prone to develop B12 deficiency[14] while a study conducted in Finnish elderly population where male gender had been observed to have increase probability for vitamin B12 deficiency[25]. In another study conducted on South Asian patients the risk appeared could be similar for men and women[24].

Limitations:

In the present study vitamin B12 measurement was used as the first-line test and the definition of vitamin B12 deficiency was based on low level of serum vitamin B12 although measurements of methylmalonic acid (MMA) and total homocysteine (tHcy) and holotrancoblamin (Holo TC) have been shown to be more sensitive in the diagnosis of vitamin B12 deficiency.

Conclusion:

Vegetarians seem to be more prone to develop vitamin B12 deficiency so they should take vitamin B12 supplement and / or B-12 fortified products to avoid its deficiency consequences.

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ORIGINAL ARTICLE

Effect of Metformin Versus Diet and Exercise on Ovulation & Menstrual Regularity in PCOS

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ABSTRACT:

Objective: To compare the effects of metformin with diet & exercise on ovulation & menstrual regularity in PCOS infertile women .
Study Design: Randomized clinical trial.
Place & Duration of study: Private hospital infertility clinic at Karachi from 2001-2004.
Patients & Methods: One hundred & eleven PCOS women with primary infertility were enrolled. and divided into group A & B with 57 & 54 patients respectively. Group A received tablet metformin 500mg thrice daily along with diet & exercise advice while group B was kept on diet & exercise alone (30-60 minutes walk daily & avoidance of oily foods, red meat & bakery products) for a period of 90 days. Menstrual regularity & plasma progesterone level were evaluated at day-0 and day-90. Fasting serum glucose, insulin, follicle stimulating hormone, luteinizing hormone, prolactin, testosterone & ultrasound pelvis were done at day- 0 for diagnosis of PCOS.
Results: 100 patients completed the study. 50 patients in each group.In group A, 44 (88%) patients developed regular cycles with statistically significant increase in serum progesterone whereas in group B only 3(6%) patients developed regular cycles with non-significant increase in serum progesterone level from day-0 to day-90. Group A showed ovulation in 82% patients in comparison to Group B where ovulation occurred in only 6% of patients.
Conclusion: Metformin produced beneficial effects in comparison to diet & exercise alone in PCOS infertile women.
Key Words: Polycystic ovary syndrome , Metformin, Diet & exercise, Menstrual regularity, Ovulation.

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a prevalent disorder that affects approximately 6-10% of women of child bearing age.[1,2]Insulin resistance and hyperinsulinemia appears to play an important pathogenic role in both obese and lean women with PCOS.[3,4,5] These women are at increased risk for type II diabetes, dyslipidemia, hypertension & atherosclerosis due to associated insulin resistance.[6,7,8]It is characterized by chronic anovulation with either oligomennorhea or amenorrhoea & hyperandrogenism.PCOS is the most common cause of anovulatory infertility.[9] There is ample evidence that hyperinsulinemia results in increased ovarian androgen biosynthesis in vivo and in vitro and decreased sex hormone binding globulin (SHBG) synthesis from the liver, leading to increased bioavailability of free androgens [10]. This excess in local ovarian androgen production augmented by hyperinsulinemia causes premature follicular atresia and anovulation [11]

Hyperinsulinemia may have a direct effect on the hypothalamus and/or pituitary to increase serum luteinizing hormone (LH) concentrations and therefore indirectly increasing LH-dependent ovarian androgen biosynthesis possibly resulting in abnormal LH and follicle stimulating hormone (FSH) release and subsequent oligomenorrhoea. Hyperinsulinemia may also directly affect the folliculogenesis and may arrest growth of antral follicles after they have reached a diameter between 5 and 8 mm.In PCOS serum concentration of estradiol lie within the normal ranges for the early follicular and midfollicular phases of the cycle[12] but the pattern of secretion differs from that in the normal menstrual cycle because there is no pre-ovulatory or midluteal increase in estradiol concentrations. The action of estradiol on the hypothalamic pituitary axis and on the endometrium is unopposed because of a lack of cyclical progesterone secretion [13].

A pathophysiologically rationalized therapeutic approach should take into account the fact that reproductive and cardiometabolic abnormalities coexist in PCOS[14]. Metformin have been introduced as a pharmaceutical option targeting not only insulin resistance (IR), but several other aspects of the syndrome including reproductive abnormalities.[15] It decreases hyperstimulation & cycle cancellations.[16]It appears to affect the ovarian function in a dual mode, through the alleviation of insulin excess acting upon the ovary & through direct ovarian effects. This later effect directly stimulates several steroidogenic enzymes in the ovary like 17α hydroxylase/ 17, 20- lyase and 3β-hydroxysteroid dehydrogenase, P450 side chain cleavage and StAR protein.[17]Insulin action on steroidogenesis at the ovary is presumed despite the co-existance of peripheral insulin resistance.[18] Lifestyle intervensions focusing predominantly on diet & physical exercise is considered the first line treatment for metabolic complications in overweight & obese women with PCOS & may have the potential to improve ovulatory function.[19] Shedding even a modest amount of weight may help.Loosing less than 10% of initial body weight has been shown to cut high levels of body fats and blood sugar. Weight loss also improves insulin resistance.[20] Thus insulin resistance & associated compensatory hyperinsulinemia play a central role in the pathogenesis of PCOS. [21]

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With this background present study was designed to evaluate the effect of metformin in comparison to diet & exercise on ovulation & menstrual regularity in patients having polycystic ovarian syndrome.

SUBJECTS AND METHODS

The clinical trial was carried out from 2001-2004 in which 111 women were selected from an infertility clinic of a private hospital at Karachi. Eligibility criteria included women of reproductive age group with ages between 20-40 years having primary infertility, oligomenorrhoea, obesity, hirsutism, fasting hyperinsulinemia (>10µU/ml) and fasting serum sugar level < 6.1mmol/L as ≥ 6.1mmol/L is WHO diabetic criteria, 2000.Consent was taken from each study participant before they were enrolled in the study.Preliminary data, date of follow up visit & laboratory investigations were recorded on a specially designed proforma. The patients were divided into two groups A & B randomly.Even number of proformas for group A (57 patients) metformin treated group & odd number of proformas for group B (54 patients) diet & exercise treated group.Tablet metformin HCl (escalation dose) was started at 500mg once daily per orally for one week & was increased to thrice daily for a period of 3months. The initial week was excluded from the study.Group B patients were advised for exercise (30-60 minutes walk daily) & change in diet pattern (avoidance of oily foods, red meat & bakery products). Menstrual cyclical changes were noted & serum progesterone was evaluated at day-0 & day-90 of the study as an indicator of ovulation (progesterone cut off value for ovulation was ≥ 4ng/ml).

Analytical method: Analysis for the serum progesterone was performed on automated random access immunoassay analysis "Immulite" from Diagnostic Product Corporation (DPC) by using commercial kits supplied by DPC.

Statistical Analysis: The observations were recorded on day 0 and day 90 for menstrual cyclical changes and serum progesterone (P). Statistical evaluation was done by using student (paired) t-test utilizing SPSS Version 10

RESULTS

A total of 100 patients completed the study period with 50 patients in each group. All patients presented in the infertility clinic with complain of no issue that is they had primary infertility. In group A out of 50 patients 35 (70%) had oligomenorrhoea & 15 (30%) had irregular cycles. In group B out of 50 patients 41 (82%) had oligomenorrhoea & 9 (18%) had irregular cycles (Table 1).

Physiological, metabolic, endocrinologic parameters along with clinical features & ultrasound pelvis were done for making diagnosis of PCOS in Group A and B (Table 2a, 2b)

In group A following 90 days of treatment with metformin 33 (66%) patients out of 35(70%) developed regular cycles, while 2 (4%) patients had no change. Out of 15 (30%) patients who had irregular cycles at day-0, 11 (22%) patients showed regularity in their cycles at day-90 while 4 (8%) patients had no change in their menstrual cyclicity. In group B after 90 days of diet & exercise treatment 39 (78%) patients out of 41(82%) had no change, while 2 (4%) patients developed regular cycles. Out of 9 (18%) patients with irregular cycles only 1(2%) patient showed regularity in cycles. (Table3).

In group A serum progesterone level showed an increase from a mean ±SD of 1.3±0.3ng/ml to 9.5±5.1ng/ml from day-0 to day-90. On statistical evaluation it was found to be significant with P-value of 0.001. In group B serum progesterone level showed an increase from a mean ±SD of 1.6±0.6 to 1.74±1.1ng/ml from day-0 to day-90. On statistical evaluation it was found to be non-significant with P-value of 0.067 (Table 4).

All patients (100%) showed increase in their progesterone level in group A but in group B 32(64%) patients showed increase, 17 (34%) patients had a decrease & 1(2%) had no change in the serum progesterone level (Table 5).

This increase in serum progesterone was divided into 2 groups (a) < 4 ng/ml and b) > 4 ng/ml. In group A 9 (18%) patients had an increase which was < 4 ng/ml while 41 (82%) patients had an increase which was > 4 ng/ml. This latter value was taken consistent with ovulation. In group B 48 (96%) patients had serum progesterone level < 4 ng/ml while 2 (6.25%) patients had an increase in level which was > 4 ng/ml. This latter value was taken consistent with ovulation (Table 6).

DISCUSSION

The etiology of PCOS remain obscure & the variability in phenotype expression continues to render the clinical care & research concerning this heterogenous condition challenging.[22]In women with PCOS the ovary does not make the hormones needed for the eggs to fully mature. Follicles may start to grow and build up fluid but none of the follicle becomes large enough. Instead some follicles may remain as cysts. Since no follicle becomes large enough and no egg matures or is released, ovulation does not occur and the hormone progesterone is not made. Without progesterone, a woman's menstrual cycle becomes irregular or ceases. In addition the cysts so produced make male hormones, which also prevent ovulation in thse women[23].

In group-A the metformin treated group 35 (70%) patients had oligomenorrhoea and 15 (30%) had irregular cycles and anovulation as confirmed by their low serum progesterone levels (mean±SD of 1.3±0.3 ng/ml). In group A 33 (66%) patients developed regular cycles after 3 months of metformin therapy while 11 (22%) patients who previously had irregular cycles experienced improvement in menstrual flow & had regular cycles. Remaining 6 patients did not had any change. Out of these 44 patients, 41 (82%) ovulated as confirmed by their serum progesterone level > 4 ng/ml. Velazquez [24] has reported the results of 22 women with PCOS completing 6 months of metformin therapy 500 mg three times per day. All patients in his study had chronic

TABLE 1
PRESENTING CHARACTERISTICS OF PATIENTS
(n=100)

S.NO	SYMPTOMS	NO. OF PATIENTS Group A	%	NO. OF PATIENTS Group B	%
1.	No issue (infertility)	50	100	50	100
2.	Oligomenorrhoea	35	70	41	82
3.	Irregular cycles	15	30	9	18

Group A= Metformin treated group Group B = Diet & Exercise treated group

TABLE 2a
BASELINE DIAGNOSTIC CHARACTERISTICS OF PATIENTS

S.NO.	CHARACTERISTICS (n=100 patients)	RANGE Group A	MEAN±SD Group A	RANGE Group B	MEAN±SD Group B
	A: Physiological				
1.	Weight (Kg)	45.0-102	69.4±11.8	52.4-92.5	75.4±8.8
2.	Height (m)	1.4-1.7	1.6±0.1	1.4-1.7	1.6±0.1
3.	BMI (Kg/m^2)	16.7-39.2	27.5±4.8	20.7-41.7	30.0±4.8
	B: Metabolic				
4.	Fasting serum glucose mg/dl)	65-110	92.74±13	75-110	92.00±11.1
5.	Fasting serum insulin (ul/ml)	10.4-51	20.6±11	10.2-30.4	18.8±5.0
	C: Endocrine				
6.	Serum progesterone(ng/ml)	0.6-1.9	1.3±0.3	0.7-3.0	1.6±0.6
7.	Serum FSH (ng/ml)	0.3-32.5	4.2±5.8	0.5-16.1	4.8±3.1
8.	Serum LH (ng/ml)	1.8-105.5	16.6±17.9	3.4-41.0	16.1±7.4
9.	Serum prolactin (ng/ml)	3.7-34.8	12.4-6.8	5.0-27.2	12.0-4.8
10.	Serum testosterone (ng/ml)	0.7-4.9	3.0±0.8	1.3-4.9	3.1±0.7

Group A= Metformin treated group Group B= Diet & Exercise treated group

TABLE 2b
BASELINE CHARACTERISTICS OF PATIENTS
(n=100)

S.NO.	CHARACTERISTICS	GROUP A (n=50)		GROUP B (n=50)	
		NO. OF PATIENTS	%	NO. OF PATIENTS	%
1.	Acanthosis nigricans	04	8	03	6
2.	Male type baldness	05	10	03	6
3.	Acne	13	26	17	34
4.	Hirsutism (face, arms & legs)	33	66	39	78
5.	Ultrasound pelvis (multiple small ovarian cysts)	37	74	39	78

TABLE 3
CYCLICAL CHANGES FROM DAY-0 TO DAY-90
(n=100)

S.NO.	CYCLICAL PATTERN	GROUP A (50)			GROUP B (50)		
		DAY-0	CHANGES	DAY-90	DAY-0	CHANGES	DAY-90
1.	Oligomenorrhoea	35 (70%)	Regular cycles	33 (66%)	41 (82%)	Regular cycles	2 (4%)
			No change	2 (4%)		No change	39 (78%)
2.	Irregular cycles	15 (30%)	Regular cycles	11 (22%)	9 (18%)	Regular cycles	1 (2%)
			No change	4 (8%)		No change	8 (16%)

TABLE 4
SERUM PROGESTERONE FROM DAY-0 TO DAY-90
(n=100)

GROUPS	CHARACTERISTICS	DAY-0 MEAN±SD	DAY-90 MEAN±SD	P VALUE
A	Serum progesterone (ng/ml)	1.3±0.3	9.5±5.1	0.001*
B	Serum progesterone (ng/ml)	1.6±0.6	1.74±1.1	0.067

* P-value significant. Using student t-test (paired) for comparison from Day-0 to Day-90.

TABLE 5
CHANGE IN SERUM PROGESTERONE AT DAY-90
(n=100)

Group	Decrease in serum progesterone		Increase in serum progesterone		No change in serum progesterone	
	No.	%	No.	%	No.	%
A (50)	0	0	50	100	0	0
B (50)	17	34	32	64	1	2

TABLE 6
INCREASE IN SERUM PROGESTERONE FROM DAY-0 TO DAY-90
(n=100)

Groups	Parameter	Sub-Groups	Change in level	Day-0	Day-90
A (50)	**Serum progesterone (ng/ml)**	A	<4 ng/ml	50 (100%)	9 (18%)
		B	> 4 ng/ml	0	41 (82%)
B (50)	**Serum progesterone (ng/ml)**	**A**	**<4 ng/ml**	50(100%)	48 (96%)
		B	**> 4 ng/ml**	0	2(6.25)

oligomenorrhoea or amenorrhoea, hirsutism and polycystic ovaries as assessed by ultrasound at baseline. Kolodziejczyk[25] and Vandermolen[26] have documented that metformin administered at a dose of 500 mg three times daily increased menstrual cyclicity and improved spontaneous ovulation. These findings are coinciding with our results whereas Acbay[27] and Ehrmann[28] have failed to demonstrate salutary effect of metformin in PCOS. In the later study the mean body mass index of the women approached 40 kg/m^2 and metformin is said to be ineffective in cases of morbid obesity.

We have observed a significant increase in the serum progesterone level from 1.3±0.3 to 9.5±5.1 ng/ml. All patients treated with metformin showed an increase with 41 (82%) patients an incline > 4 ng/ml (considered consistent with ovulation) while 9 (18%) patients showing an increase in the serum progesterone from baseline but < 4 ng/ml (considered inconsistent with ovulation). Vandermolen[26] used the serum progesterone level ≥ 4 ng/ml to determine whether participants had ovulated or not. We have also taken the same cut-off value. Velazquez[24] reported ovulation in 13 out of 15 patients with an ovulation percentage of 86.7%. All 13 patients had regular menses and serum progesterone values in the ovulatory range (3.1-28 ng/ml). Fleming[29] have found 37 out of 45 patients ovulating that is 82% ovulation rate. This is in complete accordance to our study. Jakubowicz[30] have observed a significant increase in the serum progesterone level from 70.3±5.4 to 123.7±12.4 pmol/L in 26 PCOS patients after 4 weeks of metformin therapy. All these are coinciding with our study. In contrast to this Nestler[31] has observed a decrease in the serum progesterone level from 3.1±0.3 to 2.2±0.2 mmol/L at the end of 4-6 weeks of metformin therapy. He included 31 PCOS women all having normal weight or thin built with BMI between 18 to 23.7 Kg/ m^2 whereas mean BMI in our patients was 27.5 Kg/m^2.

In group-B out of 50 patients 41(82%) had oligomenorrhoea while 9(18%) had irregular cycles. After 12 weeks of diet & exercise in the former group 39(78%) patients did not had any change while 2(4%) developed regular cycles. Whereas in the latter group with irregular cycles only 1(2%) developed menstrual cycle regularity. Moghetti et al.[32] has observed in 23 caucasian women with PCOS oligomenorrhoea in 20 (86.95%) patients & irregular cycles in 3(13%) patients which is coinciding with us. Kiddy et al.[33] found among 24 PCOS women that 11 patients lost less than 5% of their body weight & only 1(12.5%) had regularity over a 7 months period with strict low calorie diet.In our study mean weight reduction was 1.1 Kg & only 3(6%) showed menstrual regularity after 3 months of diet restriction & exercise regularly. Hutchison[34] has reported a reduction of 1.6 kg in mean body weight of PCOS kept on exercise & diet restriction which is more or less the same as our finding. However Nestler [35] has reported a non-significant increase in serum progesterone level of 12 PCOS women given placebo for 4-6 weeks. Out of 26 women only 1(4%) patient ovulated spontaneously.We have also found non-significant increase in the progesterone level of 50 women kept on diet control & exercise for 12 weeks & only 2(4%) patients ovulated in this group.

CONCLUSION

Metformin has produced beneficial effects on the reproductive function in comparison to diet & exercise alone in PCOS infertile women. It produced cyclical regularity in 88% of cases with an ovulation rate of 82% in comparison to diet & exercise treated group where menstrual regularity occured in 6% of cases with an ovulation rate of 6%. However conception rate & the live birth rate could not be ascertained in these females due to financial constraints.

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ORIGINAL ARTICLE

Association Of Vitamin D Status And Diabetes Mellitus

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ABSTRACT

Objective: To evaluate the association of 25-hydroxyvitamin D_3 (25OHD)inadequacyand hyperglycaemia in a Pakistani adult population.
Study Design: Case control study
Place & Period of Study: Department of Pathology, PNS SHIFA Hospital, Karachi; Aug 2011 to Nov 2011.
Method and Material: Plasma Glucose levels were measured in 86 patients divided on the basis of their 25-hydroxyvitamin D_3 (25OHD)levels in three groups, normal (>31 ng/ml), insufficient (20-31ng/ml) and deficient (<20ng/ml). Vitamin D insufficiency (VDI) and Vitamin D Deficiency (VDD) are collectively called Vitamin D inadequacy. 25OHD was measured by electrochemiluminescence using Roche Elecsys® Systems while glucose was estimated by routine methods on Roche Hitachi® Autoanalyser.
Results:.Vitamin D levels were inversely correlated with plasma glucose levels($r=-0.38$;$p<0.01$) with an Odd Ratio of 3.59 (95%confidence interval 1.29 to 8.70).Fasting plasma glucose was significantly higher in VDD patientsas compared to patients with normal vitamin D status ($p<0.05$).
Conclusion: Higher glucose levels were found more frequent in patients with Vitamin D deficiency.
Keywords: Vitamin D_3, Diabetes mellitus; Association; risk factor

Introduction: Vitamin D deficiency (VDD) is a world-wide epidemic with recent estimates indicating more than 50% global population at risk[1]. This pandemic of inadequate vitamin D (VDD and vitamin D insufficiency) has been found in all age groups even in those who are otherwise healthy and are not prone to deficiency[2].In Pakistan, prevalence of VDD has been reported up-to 92% in ambulatory patients in various situations[3,4]. The discovery of vitamin D receptors (VDR) in almost all the tissues has led to the identification of role of vitamin D in many organ systems of the body, instead of merely associated with bone disorders[5]. Vitamin D has also been found to play an important role in the disorders of glucose and insulin metabolism[6]. Inversecorrelation between serum vitamin D levels and glycaemic levels has been shown in many studies[5-7].Most of this data, however, pertains to Caucasian populationwhilestudies in African American have not confirmed these findings and the association between VDD and diabetes mellitus (DM) is quite blurred[8]. Asians have a high prevalence of both DM and VDD and the association of these two disorders has been described in studies carried out in Asian living in the West[9]. Vitamin D replacement therapy in South Asian patients with diabetes has also been shown to decrease HbA1c and weight[10]. Tehraniet al (2010) has shown that abnormal vitamin D concentrations were more common in South Asians with type 2 DM (T2DM) and diabetic control was inversely related to vitamin D status in South Asian women with T2DM[11]. Conversely, Taylor and Wise (1997) have reported that vitamin D replacement may increase the insulin resistance and worsen the glycaemic control in Asians[12]. Pakistan is one of the countries with a very high burden of diabetic patients and a very high prevalence of hypovitaminosis D[3,4]. So present study has been planned to evaluate an association between these two metabolic diseases.

Methods and Material: In this case control study 86subjectswere selected by non-probability convenience sampling out of the patients (mostly Armed Forces Persons and their families) referred for vitamin D estimation. Sample size wascalculated by WHO calculator taking hyperglycaemia (12%) as the least proportion outcome variable, 5% margin of error and 95% confidence interval. The subjects on vitamin D replacement therapy, patients of type1diabetes and patients with normoglycaemia as a result of anti-diabetic treatment were excluded from study. The sample population consisted of patients with normoglycaemia (NG), impaired fasting glucose (IFG), and DM. NG was defined as Fasting Plasma Glucose (FPG)< 5.6 mmol/L, IFG: 5.6 – 7.0 mmol/L and DM> 7.0 mmol/L[13]. Similarly, on the basis of their 25OHDlevels in blood the subjects were clustered in three groups, normal (>31 ng/ml), insufficient (20-31ng/ml) and deficient (<20ng/ml)[14]. 25OHD was measured by electrochemiluminescence using Roche Elecsys® Systems while glucose were estimated by routine methods on Roche Hitachi®

Statistical Analyses: The data was recorded in SPSS version 17 and frequencies of various groups of subjects according to Vitamin D status were determined. Comparison of frequencies was carried out usingChi Square test, while continuous data i.e. Plasma glucose and 25OHDwas compared by students` t test. Then correlation studies were carried out between FPG and

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25OHD levels using Pearson`s Correlation Coefficient. VDD and vitamin D insufficiency (VDI) of vitamin D status groups were combined and IFG and DM of glucose categories were combined and then 2x2 table was constructed for comparison and calculation of Odd Ratio (OR) using chi-square test.

Results: The sample population had a slight female preponderance (53%), while median age was 34 years (range: 19- 65 years). Vitamin D inadequacy was found in 27 (31%) subjects. DM was more frequent in subjects with VDD (50%i.e. half of the patients with VDD were also having DM) and VDI(31.6%) as compared to subjects with normal vitamin D status (6.1%)(Table 1).Similarly, more patients with IFG were found in VDD (25%) and VDI (26.3%) groups as compared to subjects with normal Vitamin D status. Gradual worsening of glycaemic condition was found on progressing from normal vitamin D status to insufficiency and deficiency (Figure1).Plasma glucose was significantly higher in VDD patientsas compared to those subjects with normal vitamin D status ($p < 0.05$) (Table 2). Vitamin D levels were inversely correlated with plasma glucose levels ($r=-0.38$;$p< 0.01$) (Table 2). Table 3 shows that Vitamin D inadequacy in normal and abnormal glucose groups (OR: 3.59; 95% confidence interval 1.29-8.70

Discussion: The association of Vitamin D and DM has been described for more than twenty five years now[15]. Many workers have shown evidence that vitamin D is related to various aspects of glucose metabolism e.g. improving beta-cell function of pancreas, insulin secretion and insulin sensitivityand is one of the most important environmental factors causing T2DM[16-20]. Our data has shownttwo significant findings i.e. higher prevalence of IFG and frank DM in patients with VDI and VDD, and a significance correlation of FPG and vitamin D levels. Many cross-sectional studies carried out in Western populations havegenerally reported an inverse association between vitamin Dstatus and prevalent hyperglycemia[21].Similar associations between higher fasting plasma glucose levels and vitamin D status were observed in a community-based study of older adults without known diabetes[22]. Expressing this association in another manner, Tahrani et al (2010) has shown that a low serum 25OHD(< 20 ng/ml) was more common in diabetics as compared to controls (83% vs. 70%; p <0.07)[11]. In another study from US, mean25OHDlevels among T2DMpatients were found significantly lower than in individuals without T2DM(OR 1.85; 95% CI 1.03 – 3.32; P = 0.038)[23]. Conversely, in an Indonasian study 81% diabetic were found to be having VDD as compared to 75% non-diabetic (OR: 0.8; 95% CI 0.42 – 1.21; P = 0.46)[24] whereas our study showed an OR of 3.35 (95% CI: 1.29-8.70). This discrepancy is difficult to explain but is probably due to difference in age of the selected population.

Theclose association between vitamin status and DM has been further emphasized by the finding that inadequate vitamin D level is an important risk factor for the development of type 2 DM[25-28]. The intervention studies to improve glycaemic control with certain doses of vitamin D, however, have shown variable results[29-30].Beneficial effectof vitamin D on T2DMis needed to be confirmed in large trialsspecifically designed to test the hypothesis that vitamin Dstatus is a direct contributor to the pathogenesis of T2DM.If such an intervention is clearly shown to be effective this could have substantial public health implications[21].

This was among the initial studies in our countryto examine the association of vitamin D status with various categories of glucose abnormalities but with some limitations e.g. impaired glucose tolerance which is a category of hyperglycaemia based on oral glucose tolerance test could not be studied. Similarly data regarding glycosylated hemoglobin could not be recorded.

Conclusion:A significant associationbetween diabetes mellitus and vitamin D inadequacy exists which imply that vitamin D deficiency or insufficiency is undesirable in patients with any form of hyperglycaemia.

Table 1: Distribution of various glycaemic groups in subjects with different Vitamin D Status

Vitamin D Status	No of subjects (n=86)	Normoglycaemia (FPG < 5.6 mmol/L)	IFG (FPG 5.6 – 7.0 mmol/L)	DM (FPG > 7.0 mmol/L)	Significance levels (Chi Square Test)
Normal (>30ng/ml)	n=59	45 (76%)	11(18.6%)	3 (5.1%)	Normal and Insufficiency Group (p= <0.001)
Insufficiency (20-30ng/ml)	n=19	8 (42.1%)	5 (26.3%)	6(31.6%)	Insufficiency and Deficiency Group (p= <0.001)
Deficiency (<20 ng/ml)	n= 8	2 (25%)	2 (25%)	4 (50%)	Normal and Deficiency Group (p<0.001)

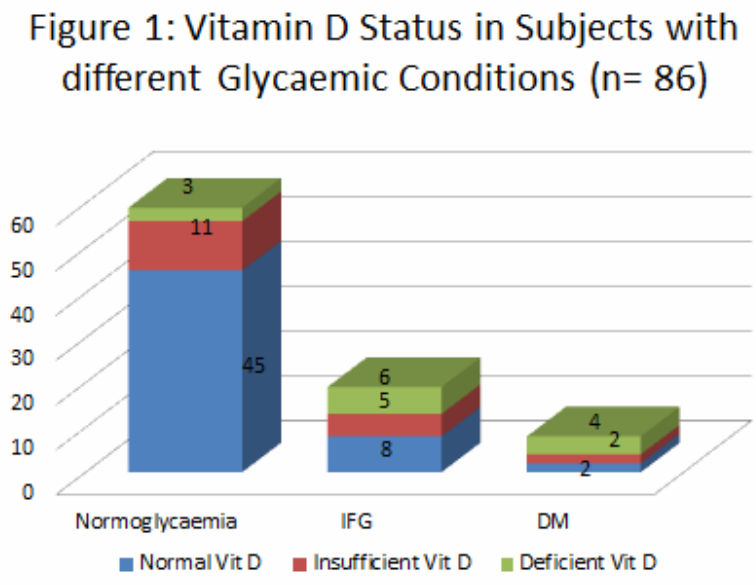
FPG: Fasting Plasma Glucose, **IFG:** Impaired Fasting Glycaemia, **DM:** Diabetes Mellitus

Table 2 :Comparison of Fasting Plasma Glucose Levels in various groups of Vitamin D Status and Correlation Studies between FPG and Vitamin D Levels

Inferential Statistics				Correlation Studies	
Vitamin D Status	**No of subjects (n=86)**	**FPG (mmol/L) (mean±SD)**	**Significance levels (independent t test)**	**Pearson`s Correlation (r-value)**	**Significance level (P value)**
Normal (>30ng/ml)	n=59	5.4±2.2	Normal and Insufficiency Group (p= NS)	r= -0.38	P <0.001
Insufficiency (20-30ng/ml)	n=19	6.3±2.3	Insufficiency and Deficiency Group (p= NS)		
Deficiency (<20 ng/ml)	n= 8	8.1±3.8*	Normal and Deficiency Group (p<0.05)		

Table 3: **Risk Estimate of Vitamin D adequacy in Normal and abnormal glucose levels**

	OR	95% Confidence Interval	
		Lower	Upper
Odds Ratio for Glucose level (Normal / abnormal)	3.359	1.297	8.701
N of Valid Cases	86		



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Student's Corner

Study On Pattern Of Obsessive Behaviors And Thoughts In A State Of Anxiety In Teenagers

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Abstract:
Objective: To determine pattern of obsessive behaviors and thoughts in a state of anxiety in teenagers (14-18 years) of age.
Study Design: Cross sectional
Methods: We conducted research on teenagers of different cities of Pakistan. We selected about 100 student s of age 14-18 years, out of which 55 were girls and 45 were boys of schools, colleges and academies. DASS (depression anxiety stress scale) was used as instrument.
Results:
Our study showed that 30 students (30%) felt that everything was alright and nothing bad will happen at any time. Similarly same number of teenagers was never afraid for any reason in their day to day lives. We found that about 24(24%) never had any frightened feeling whereas about same number had flushing of face in embarrassing situation sometimes. About 18(18%) teenagers complained of worrying thoughts sometimes at night whereas about same number had a good night sleep all of the time. About 38 teenagers (38%) neither faced difficulty in swallowing in a tense situation nor did they avoid eating in public places in a similar situation. Many students felt afraid of participating in extracurricular activities i.e. about 24 students (24%). However they willingly participated in group discussions. About 55 students (55%) were neither afraid of participating in group discussion nor in extracurricular activities.
Conclusion**:**
Obsessive behaviors and thoughts were uneasy feelings (like butterflies) in stomach, hot and flushed face, feeling frightened or scared, worrying thoughts at night and difficulty falling asleep.
Key words: Anxiety, depression, obsessive thoughts.

Introduction

Anxiety is a future oriented psychological and physiological mood state characterized by cognitive, somatic, emotional and behavioral components, which create unpleasant feelings. These problems can become chronic or recurrent, substantially impairing an individual's ability to cope with feelings of daily life[1].

Scientific studies have shown that feelings of anxiety are accompanied by physiological activity, also known as arousal, in a person's sympathetic system. This activity or arousal, when moderate may cause an individual to feel physical tenseness, nervousness or restlessness.

Research has shown that certain parts of brain such as Amygdala in temporal lobe become activated when an individual experiences anxiety [2]. The hippocampus and amygdala are major nuclei of Limbic system, a pathway known to underlie emotions[3].These centers in turn activate hypothalamic pituitary axis (HPA) [3]. There are many neurotransmitter alterations in Anxiety disorders[3]. In keeping with the broader view of anxiety atleast five neurotransmitters are disturbed in Anxiety: serotonin, norepinephrine, gamma aminobutyric acid(GABA) and corticotropin releasing hormone(CRH) and cholecystokinin[3]. There is such careful orchestration between these neurotransmitters that change in one neurotransmitter invariably elicit changes in another including extensive feedback mechanisms[3]. Serotonin and GABA are inhibitory neurotransmitters that quiet the stress response[4].

Low level of GABA, a neurotransmitter that reduces activity in CNS, contributes to anxiety. A number of anxiolytics achieve their effect by modulating GABA receptor [5, 6, 7.]

Obsessive compulsive pathology is characterized by intrusive thoughts about potential danger and a compulsion to engage in stereotyped activities. In neurophysiological terms OCD stems from a dysfunction of a specific brain circuit, the cortical-striato-pallidal thalamic circuit and particularly a dysfunction of basal ganglia[8]. There seems to be reduced inhibition of strongly motivated routines (washing, cleaning, checking one's environment, monitoring other agents' behavior) initiated in the striatum, because striatal networks to cortical input and/or because their inhibitory effect on thalamic networks is diminished[8].

There are several types of anxiety disorders, including panic disorder, obsessive-compulsive disorder, and post traumatic stress disorder (PTSD), social anxiety disorder, specific phobias and generalized anxiety disorder (GAD) [9.]

Individuals with Obsessive-Compulsive disorders have thoughts that will not go away or feel they must perform behaviors over and over again. People with obsessive personalities may refuse to leave their homes because of persistent thoughts that they will kill someone and compulsive personalities may wash their hands a hundred times a day in order to get rid of germs. Unlike the other anxiety disorders, post-traumatic stress disorder is caused by exposure to a traumatic event such as a natural disaster, repeated child abuse[10].

Other anxiety disorders are characterized by different symptoms. For example, individuals with panic disorder experience a sudden onset of intense terror, and may suffer from an impending feeling of sadness. Individuals

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who suffer from this disorder may experience severe chest pains, dizziness, shortness of breath, trembling and sweating. Some experts say that biological factors may play a role in panic disorders.

Individuals with a phobic disorder have an unexplainable, irrational awful and persistent fear of a particular object or situation. Individuals with phobia disorders will go to almost any lengths to avoid the thing that scares them.

GAD involves uncontrollable and unrealistic worry about every day situations such as most schoolwork, relationship or health. This worrying has to occur on most days for at least six months for a diagnosis of GAD[11].

It is commonly seen that when teenagers suffer from anxiety disorder their thinking, decision making ability, perception of environment, learning and concentration towards their studies and their other activities get affected. They not only experience fear, nervousness, and shyness but also start avoiding people and activities. If they are left untreated, they face different risks such as poor results at school and avoidance of important social activities.

Teenagers who suffer from an anxiety disorder could suffer from other disorders such as depression, eating disorder, attention deficit disorder both hyperactive and inattentive.

However, researchers also agree that a moderate degree of anxiety may well motivate the student and encourage him/her towards better academic achievement[12]. Hence, some degree of anxiety is considered a necessity for learning and high academic achievement. The contrary is unfortunately also true, as a high anxiety score may be a severe obstacle to academic achievement[3].

In recent years, anxiety disorders have been found to be increasingly prevalent, and the burden of illness associated with these disorders is often considerable.

Pakistan has a total population of about 160 million. The total number of psychiatrists for such a large population is only 250[13].

Available research suggests that social problems are major cause for anxiety and depressive disorders in Pakistan, and it has an overall prevalence of 34%[14]. Socio demographic factors associated with increased prevalence of anxiety and depressive disorders were female sex, middle age and low level of education. Loss of husband (being widowed, separated or divorced), increasing duration of marriage and being a housewife were also positively associated[4].

Rationale

Teenagers are backbone of our country. Progress and prosperity of a country depends on them. Unfortunately due to many reasons anxiety is rising among them, so we wanted to have a look at the pattern of negative thoughts

There were about13 respondents (13%) who were confident enough to look into eyes of strangers and their heart beat always kept at normal pace when seeing strangers.

in a state of anxiety among youngsters. To the best of our knowledge this work has not been done in our background.

Objective

To determine pattern of obsessive behaviors and thoughts in a state of anxiety in teenagers 14-18 years of age.

Subjects and methods

We used DASS (Depression Anxiety Stress Scale) to assess anxiety level. The instrument comprises of 42 self reported items.

We selected students according to our own convenience. Interviews were conducted during students' recess time and were self reported.

Data entry and analysis was done on SPSS version 15.0

Inclusion criteria

Healthy teenagers aged 14-18 years (both girls and boys)

Exclusion criteria

Those suffering from any acute or chronic disease

Sample size

Considering a prevalence (p) of 34%[14], and a bound on error (e) of 5%, we calculated our sample size as follows

$S = z^2pq/e^2 = (1.962 \times 0.3 \times 0.7)/ (0.05)2 = 323$

Our sample size came out to be 323 but practically we collected data on 100 students so as to complete within time.

Study design

Cross sectional

Results

In our study we found that there were about 45(45%) male and about 55(55%) female students. About 23(23%) were 18 years of age (table1).

From our study we came to know that about 30 students (30%) were those who felt that everything was alright and nothing bad will happen all of the time(table 2). Similarly same numbers of teenagers were never afraid for any reason in their day to day lives (table 2).

We found that about 24(24%) never had any frightened feeling whereas about same number had flushing of face in embarrassing situation sometimes (table 2).

About 18(18%) teenagers complained of worrying thoughts sometimes at night whereas about same number had a good night sleep all of the time (table 2).

About 38 teenagers (38%) neither faced difficulty in swallowing when they were caught in a tense situation nor did they avoid eating in public places in a similar situation.

Many students felt afraid of participating in extracurricular activities i.e. about 24 students (24%). However they willingly participated in group discussions. About 55 students (55%) were neither afraid of participating in group discussion nor in extracurricular activities

About 17 teenagers (17%) messed up their things when they were in a tense situation, similar number got upset easily and felt panicky sometimes.

Table 1: Age of subjects

Age (years)	Frequency(n)	Percentage
18	23	23
17	14	14
16	28	28
15	20	20
14	15	15

Table2: Frequency of obsessive behaviors and thoughts

Variable	1	2	3	4	Total
Feeling everything is all right	Sometimes	Rarely	All of the time	Never	
	4	1	1	26	32
	2	1	0	8	11
	2	2	3	30	37
	4	3	1	12	20
Feeling afraid for no reason	4	2	2	4	12
	1	1	2	3	7
	1	0	3	1	5
	26	8	30	12	76
Feeling butterflies in stomach	5	1	5	5	16
	4	2	5	1	12
	1	1	10	1	13
	24	1	18	16	59
Hot and flushed face	5	4	1	24	34
	1	2	1	1	5
	5	5	10	18	38
	5	1	1	16	23
Worrying thoughts at night	18	4	11	6	39
	9	0	6	1	16
	3	4	16	3	26
	4	1	14	0	19
Easily fall asleep at night and	18	9	3	4	34
a good night sleep	4	0	4	1	9
	11	6	16	14	47
	6	1	3	0	10

Discussion

For our study we chose to select an equal number of students in terms of gender. However other studies say that females are more anxious as compared to males[12]. Other risk factors besides female gender were found to be middle age, low level of education, financial difficulty, being a housewife and relationship problems[12]. Also it was found that those people having close confiding relationships were less likely to have anxiety and depressive disorders[4].

Most of these students enjoyed their sleep at night and did not have any worries in their mind during their sleep thus representing a healthy group of teenagers. Sleep and mood are closely connected; poor or inadequate sleep can cause irritability and stress, while healthy sleep can enhance well being[15]. Studies have shown that even partial sleep deprivation has a significant effect on mood. University of Pennsylvania researchers found that subjects who were limited to only 4.5 hours of sleep a night for one week reported feeling more stressed, angry, sad and mentally exhausted. When the subjects resumed normal sleep, they reported a dramatic improvement in mood[16].

Not only does sleep affect mood, but mood and mental states can also affect sleep. Anxiety increases agitation and arousal, which makes it hard to sleep. Stress also affects sleep by making the body aroused, awake and alert. People who are constantly under stress tend to have sleep problems. Difficulty sleeping is sometimes the first symptom of depression. Studies have found that 15-20% of people diagnosed with insomnia will develop major depression.

Sleep problems may in turn contribute to psychological problems. For example chronic insomnia may increase an individual's risk of developing a mood disorder, such as depression or anxiety. In one major study of 10,000 adults, people with insomnia were 5 times more likely to develop depression[17]. Lack of sleep can be an even greater risk factor for anxiety. In the same study, people with insomnia were 20 times more likely to develop panic disorder (a type of anxiety disorder) [17]. Another study showed that insomnia is a reliable predictor of depression and many other psychological disorders including all types of anxiety disorders[18].

Most of them did not face any difficulty in swallowing when they were tense neither did they avoid eating in public places. Difficulty in swallowing is thought to be a common physical symptom of anxiety. Globus hystericus is the correct term for this symptom. It is caused by the muscles in the throat contracting due to anxiety or stress. This is another example of a symptom which will improve if it is given no credibility. It is totally harmless and will not cause cessation of breathing, eating or drinking[19].

It is well known that participation in sports or other activities besides academics plays a positive role in teenagers. Hence school assimilation is essential for students with anxiety. In our study most of them liked to participate in sports and group discussions. Participation in athletic activities can be a buffer to stress and anxiety. Allowing students to share common experiences and to work in groups can help them adjust during years in college.

Our teenagers did not face any trouble when seeing strangers. This again shows a positive and healthy sign of our teenagers. Stranger anxiety is an innate anxiety, mistrust or wariness of foreigners, newcomers, outsiders or other unacquainted and unknown individuals. Social anxiety is more common in children and infants.

Our research strengthens the idea that negative thoughts can drive people or teenagers into anxiety and low mood[11].

On the other hand it is seen that positive behavior or positive thought plays a positive role in relieving anxiety and stress. Cognitive behavior therapy[20] is thus found to be most effective in alleviating anxiety. Cognitive therapy is a treatment process that helps patient's correct false self beliefs that lead to certain moods and behaviors. The fundamental principle behind this therapy is that thought precedes a mood, and that both are interrelated and a person's environment, physical reaction and subsequent behavior. Therefore changing a thought that arises in a given situation will change mood, behavior and physical reaction.

Conclusion

We looked at various obsessive behaviors and thoughts during anxious state in teenagers. Some common obsessive behaviors and thoughts were uneasy feelings (like butterflies) in stomach, hot and flushed face, feeling frightened or scared, worrying thoughts at night and difficulty falling asleep.

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Case Report

A Case of Subhyaloid Haemorrhage Managed with ND:YAG Laser Hyaloidotomy

Muhammad Waseem, Tariq Shakoor, Saquib Naeem, Muhammad Saleem Bajwa

Abstract:
Subhyaloid hemorrhage is rarely seen in ophthalmological practice in young males. We managed one such case in our set-up. A young male presented with sudden decreased vision. Fundus showed large collection of darkish red colored blood in subhyaloid space of the posterior pole in front of the macula, typical of sub-hyaloid hemorrhage. Treatment includes, amongst others, Nd: YAG laser hyaloidotomy. Prognosis, if treated on appropriate lines, is usually good. This case was being reported for general awareness.
Key-words: Nd: Yag laser hyaloidotomy, premacular sub-hyaloid haemorrhage

INTRODUCTION

Subhyaloid haemorrhage, also called preretinal hemorrhage is a collection of blood between the retina and posterior vitreous face It is a rare entoty. Various causes are trauma, Valsalva retinopathy, shaken baby syndrome and macroaneurysm. It is usually unilateral disorder. Clinical features and course depend upon the volume and causes of the hemorrhage. Symptoms include sudden painless loss of central vision with some spared periphral vision. Fundus usually shows the boat-shaped hemorrhage obscuring the retina but can be circular due to massive bleed. In some eyes, blood becomes compacted in the posterior gel to form an 'ochre membrane' Fundus fluorescein angiography may shows presence of vascular anomaly. Smaller hemorrhage resolve spontaneously in a month or two but massive hemorrhages need active treatment which includes pars plana vitrectomy, tissue plasminogen activator and injection of perfluoropropane. Prognosis usually remains good in minor bleeds but may cause permanent visual loss in large cases 1-5.

Case report: A 32 years old male reported in CMH Hyderabad on 10th March 2012 with sudden, painless loss of vision in right eye of one week duration. He had a history of strenuous physical work few hours prior to the development of visual complaint. He was seen by the eye specialist. Vision in right eye was only perception of hand movements at 30 cm. Other general physical, systemic and ophthalmic parameters were normal. Fundus examination showed extensive Pre- retinal (subhyaloid) hemorrhage. It was about 7 disc diameter and upper border was beyond the superior temporal vascular arcade while lower border was within inferior temporal arcade. He was investigated. His blood picture, platelet count, urine report, lipid profile, blood sugar, liver function tests, VDRL, RA factor and antinuclear factors were normal. He was referred to eye department PNS Shifa, a tertiary care hospital, by the eye specialist of CMH Hyderabad on 27th March 2012 for further management

Fundus photographs taken in PNS Shifa on 28th March 2012 are shown in Fig.1.Nd:YAG laser posterior hyaloidotomy was done at the most dependant and most bulging part of lesion on the same day, using fundus contact lens, energy level of 1.2 mJ/pulse and spot size of 150 microns. 3 shots were sufficient to cause significant hole to drain the blood out. Short tapering course of systemic steroids was given, starting from Tablet Prednisolone

30 mg a day in divided dosage which completed in 2 weeks. Fundus photographs taken after 5 minutes, 20 minutes, and on 16th day (i.e., on 13th March 2012) are shown in Fig.2, 3 and 4 consecutively. Optical Coherence Tomography (OCT) showed separation of internal limiting membrane (ILM) from the retina (Fig.5.). Fundus fluorescein angiography was done and found to be inconclusive due to some blood along the superior temporal arcade. Vision was restored to 6/6 in right eye. Patient was given prophylactic Argon laser photocoagulation along the borders of the (previous) subhyaloid hemorrhage. He was discharged on 13th April 2012 with advice to avoid strenuous physical work in future and a regular follow up.

Discussion:

Our patient had extensive and a month long-standing Subhyaloid (preretinal) hemorrhage. Chances of auto-absorption without macular dysfunction were very less. So to avoid permanent damage to the macula, we resorted to the drainage of the blood through Nd: Yag laser hyaloidotomy, which is considered a safe procedure as compared to pars plana vitrectomy. Patient usually recovers quickly. We used only 3 shot of 1.2 mJ per pulse Nd:YAG Laser energy which was significantly less than that used by Durkan 5. The reason may be the use of different fundus contact lens or difference in expertise and precision. The Khadka investigated the effects of Nd: YAG Laser hyaloidotomy, having pre-macular hemorrhage in acute childhood leukemia and found good results in 9 out of 11 eyes6,7 . However our patient was young adult and not having any obvious

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systemic ailment. If started at an early stage, long-term result seemed to be very good8. Our patient did not develop any complication so far. We would like to follow this case at least for 1 year.

Conclusion

Subhyaloid (preretinal) hemorrhage may be dealt according to the size, duration and etiology of the hemorrhage. Nd: YAG laser is a comparatively recent relevant therapeutic modality. Result of the treatment is fruitful if detected early and treated properly

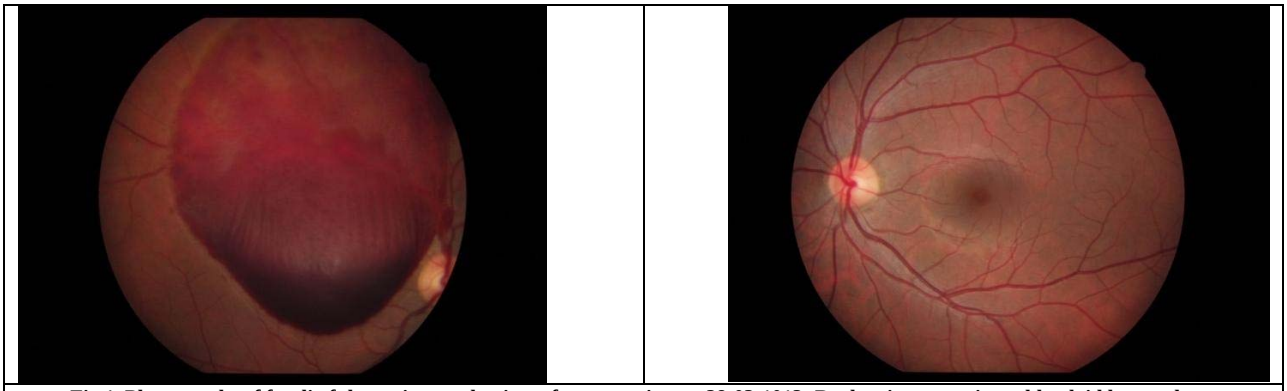

Fig.1. Photographs of fundi of the patient at the time of presentation on 28-03-1012: Rt showing extensive subhyaloid hemorrhage

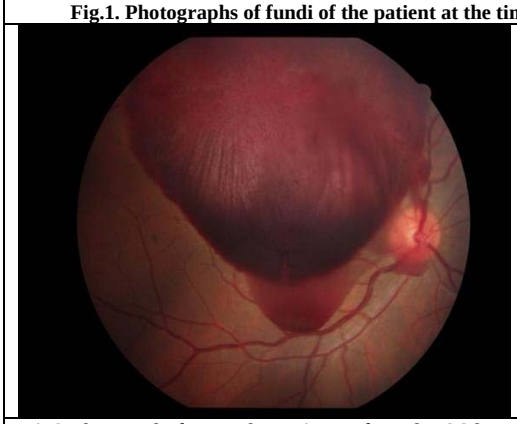

Fig.2. Photograph of Rt Fundus 5 minutes after Nd: YAG laser hyaloidotomy showing initial drainage of blood from subhyaloid space

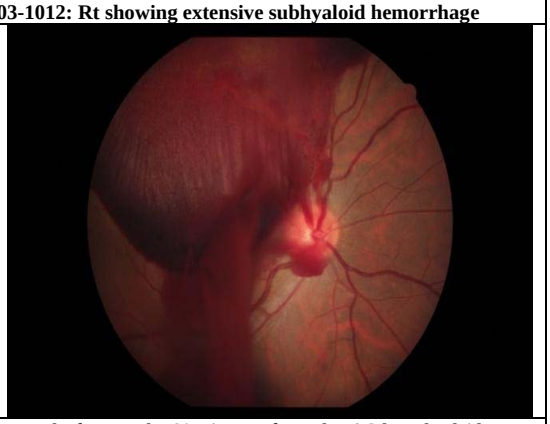

Fig.3. Photograph of Rt Fundus 20 minutes after Nd: YAG laser hyaloidotomy showing more drainage of blood from subhyaloid space.

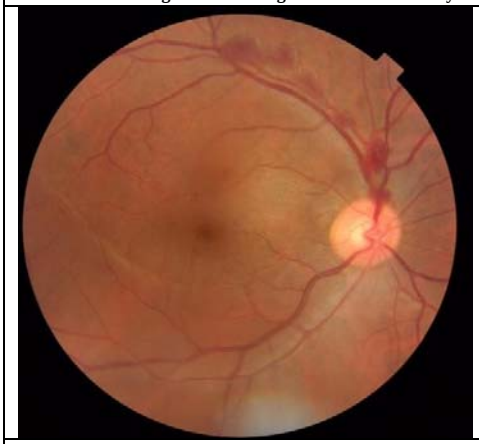

Fig.4. Photograph of Rt Fundus 16 days after Nd: YAG laser hyaloidotomy showing almost complete clearing of blood from subhyaloid space and restoration of vision to 6/6.

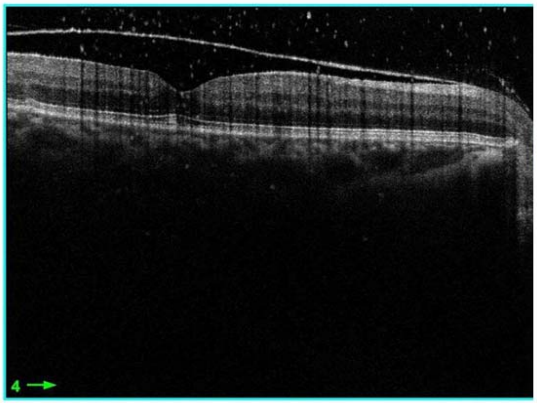

Fig.5. OCT of Rt Fundus 16 days after Nd: YAG laser hyaloidotomy showing separation / detachment of ILM.

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