

FREQUENCY OF VITAMIN D DEFICIENCY IN PATIENTS WITH FATIGUE.

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ABSTRACT:

OBJECTIVE:

To study vitamin D status in patients presenting with complaint of easy fatigability and also its prevalence in relation to common contributors to this complaint which may manifest without any physical sign e.g. new onset Diabetes mellitus and Chronic Hepatitis B and C.

SETTINGS AND DURATION:

This descriptive study was conducted at medical outpatient clinic at Chinniot General Hospital and Madinah Teaching Hospital from March to May 2012 in patients coming from Faisalabad and its suburbs.

MATERIAL AND METHOD:

This study included 100 patients with age limit 16 to 60 years. Sample population included only those patients who neither had a known disease, physical or psychological nor any sleep disorder that could contribute to their complaint of easy fatigability. Organic diseases that could contribute to fatigue were carefully ruled out by clinical examination. For each patient, random blood glucose level, hepatitis B surface antigen (HBsAg) and hepatitis C antibody (anti HCV) and 25Hydroxy D levels (25OHD) were done.

RESULTS:

Out of 100 patients, 92 were found to have low Vitamin D levels. Only 8 were found to have Vitamin D status in the normal range and these included all females. 86 patients were Vitamin D deficient, one third of who in were having severe deficiency with almost equal gender distribution. Among Vitamin D deficient cases, 2/3rd belonged to female gender. 6 patients had vitamin D insufficiency and none had vitamin D level above the normal range. Furthermore, none had optimal Vit D level.

Only 18 patients were found to be anti HCV positive and 12 patients were HBsAg positive, both with equal gender distribution.

High blood glucose level was observed in 12 patients out of whom, 75% were found to have random blood glucose level > 200mg /dL and rest had impaired glucose tolerance.

CONCLUSION:

Prevalence of Vitamin D deficiency is alarmingly high in patients presenting with fatigue, even more than that seen in other parts of the world. Furthermore relative frequencies of Chronic Hepatitis B & C and Diabetes mellitus are much less as compared to that of vitamin D deficiency, despite Pakistan being declared a "cirrhotic state" where Diabetes mellitus is an "epidemic".²⁸

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INTRODUCTION:

Complaint of easy fatigability is more common these days than ever before. One can talk to any patient or seemingly healthy person and will find complaints of lethargy and poor stamina. This phenomenon is on the rise.

Important diseases that can cause fatigue include endocrine illnesses like thyroid dysfunction, diabetes mellitus, and chronic diseases such as chronic obstructive airway disease, chronic infections (e.g. chronic hepatitis, infective endocarditis), congestive cardiac failure, anemia autoimmune disorders and neoplasia. Alcoholism and certain drugs like sedatives and Beta-blockers can also cause similar clinical picture. Lastly, psychological conditions such as fibromyalgia, depression and sleep disorders etc. can also cause lethargy and body aches.^{2,8,22}

Fatigue of unknown cause or related to psychological illness exceeds that secondary to physical ailment and drugs.¹⁰

In recent times, hazards of vitamin D deficiency are in the limelight in clinical research. Vitamin D deficiency is not only associated with metabolic bone disease such as Osteomalacia and rickets but it can present with easy fatigability without evidence of osteopenia. It works at mitochondrial level in myositis, impairing cellular respiration thereby causing fatigue.^{16,24} Many cases labeled as fibromyalgia were actually found to have vitamin D deficiency, so it remains a diagnosis of exclusion.^{9,21}

Vitamin D, also called "Sun vitamin", is a hormone produced in our skin following exposure to sunlight in its primitive form called as Provitamin D (7 deoxy cholesterol) which under goes hydroxylation first in the liver and then in the kidneys to produce active form of vitamin D (1, 25 dihydroxy cholecalciferol). This is the most important source of vitamin D for humans.²⁰ Other sources of vitamin D include mushrooms and oily fish. Excessive cooking spoils vitamin D content in these sources.^{14, 15} This active form of Vitamin D in turn causes increased absorption of calcium and phosphate from the gut and suppresses parathyroid hormone.

Vitamin D deficiency has been defined as levels below 20 ng/ml, whereas anything between 21 and 29 ng/mL is called *vitamin D insufficiency*. *Optimal vitamin D levels* are between 40 and 60 ng/mL and anything above 150 ng/mL is considered to be *vitamin D toxicity*. *Normal vitamin D level is between 30-100 ng/mL.*²⁷

Vitamin D deficiency is a global phenomenon. It has been estimated that in Europe, USA and Canada; 20-100% elderly population is vitamin D deficient.¹¹ Children and adults are at equally high risk of developing vitamin D insufficiency and deficiency worldwide.¹² Replacement of vitamin D results in significant decrease in level of intensity of body aches.^{1, 4} WHO recommends at least 30 minutes sun exposure daily for optimal vitamin D status in adults. Furthermore, daily intake of vitamin D from various food sources should increased at least twice the recommended intakes for western population.^{25,26} Vitamin D intake above the dietary reference range is not associated with increased risk of adverse events and so is the protected sun exposure.^{1,21}

Scarcity of local published data regarding vitamin D status prompted us to conduct this study in adults from Faisalabad and its suburbs, which were without any psychological or physical ailment and sleep disorder, yet complaining of easy fatigability. It is especially important to study relative place of vitamin D deficiency as a cause of easy fatigability in the perspective of Chronic Hepatitis B and Diabetes mellitus which like vitamin D deficiency, do not have any clinical sign at an earlier stage.

METHODOLOGY:

This descriptive study involved 100 patients attending evening medical OPD at Chinniot General Hospital and Madinah Teaching Hospital, Faisalabad. It was conducted from March to May 2012.

Inclusion Criteria:

It included adult patients aged between 16 to 60 years from Faisalabad city and its suburbs, presenting with fatigue of not less than 2 month duration.

Exclusion Criteria:

Patients suffering from any organic illness apparent clinically, psychiatric illness and insomnia that can cause easy fatigability were excluded on clinical grounds.

All the patients included in the study were not previously known for their hepatitis and diabetes status.

Statistical analysis was carried out on SPSS 17. The base line difference between patients with mild, moderate and severe deficiency of 25OHD level was determined. Co-relation between gender and vitamin D was determined. Demographic data pertaining to vitamin D status were collected. Serum 25OHD levels carried out on Advia centaur instrument employing chemiluminescent micro particle immunoassay (CMIA). HBsAg and Anti HCV status were done using ELISA technique. Random blood glucose levels were done using micro lab model 300 (Merck).

RESULTS:

Our study revealed that majority of patients complaining of easy fatigability had low vitamin D level. Vitamin D status was further classified as severe deficiency, deficiency, insufficiency, normal, optimal and toxicity.

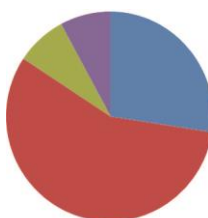
Study revealed that 92% patients had low vitamin D levels. 28% patients had severe deficiency which constituted almost 1/3rd of total number of patients with predominant female distribution. 6% patients had insufficient vitamin D levels and 8% had normal levels and all belonged to female gender. There was not a single patient having optimal vitamin D status or achieving toxic levels. Mean vitamin D levels were 14.32 ng/mL for females and 11.52ng/mL for males showing overall vitamin D deficiency for both genders.

12% of the patients were HBsAg positive with equal gender distribution. Whereas 18% patients were anti HCV positive and all belonged to female gender. High blood glucose level was observed in 16% patients of whom 75% were found to have levels > 200mg/dL.

Table: VITAMIN D STATUS (Total)

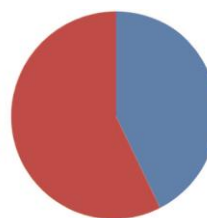
Gender	Vitamin D Status (%)					
	Severe deficiency	Deficiency	Insufficiency	Normal	Optimal	Toxicity
Male n=28	12 (42.8%)	16 (57.2%)	0	0	0	0
Female n=72	16 (22.2%)	42 (58.3%)	6 (8.3%)	8 (11.2%)	0	0
Total n=100	28	58	6	8	0	0

Vitamin D status (Male)



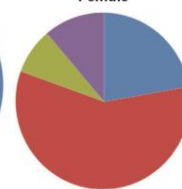
■ Severe vitamin D deficiency
■ Vitamin D deficiency
■ Vitamin D insufficiency
■ Normal vitamin D level
■ Optimal vitamin D level
■ Vitamin D toxicity

Vitamin D status (Female)



■ Severe vitamin D deficiency
■ Vitamin D deficiency
■ Vitamin D insufficiency
■ Normal vitamin D level
■ Optimal vitamin D level
■ Vitamin D toxicity

Female



■ Severe vitamin D deficiency
■ Vitamin D deficiency
■ Vitamin D insufficiency
■ Normal vitamin D level
■ Optimal vitamin D level
■ Vitamin D toxicity

DISCUSSION:

The study revealed that majority of patients with fatigue had low vitamin D levels. This favors international and national literature on the subject. A German study by Merlo C et al showed frequency of vitamin D deficiency to be 45% in patients at a primary care clinic.¹⁷ Another European study from Norway by Knutsen KV et al in multi ethnic general practice reported vitamin D deficiency in 58% of patients. In these, 1/3rd of ethnic Norwegians and 83% of patients from Middle East, Africa and South Asia had low vitamin D levels.³ Baig A et al, in patients visiting Abbasi Shaheed Hospital Karachi, showed frequency of vitamin D deficiency to be 92%.¹⁹ This is the same figure as present study revealed. A similar percentage (92.85%) was recorded by Aslam M et al in their study from Faisalabad conducted in an antenatal clinic.⁵ Another study on adult

patients from Northern Pakistan by Mufti MA et al, visiting medical outpatient department of Shifa International Hospital, Islamabad showed low vitamin D levels in 89.3% patients with vitamin D deficiency in 73.2% and insufficiency in 16.1%.²⁰ Data from neighboring countries of Pakistan in South Asia showed similar figures regarding vitamin D deficiency. Habit of chewing betel nut has been incriminated for this by modulating the activity of enzymes which regulate circulating levels of 1,25 OH D.²³ Asians with pigmented skin despite having immense sun exposure, have much less vitamin D levels as compared to European and American population.^{19, 27} This can be explained by the fact that high degree of pollution prevents ultra violet rays from penetrating the human skin.^{13, 14} In addition, dark skin tone in Asians also prevents absorption of these rays contributing to impaired synthesis of active form of vitamin D in human skin.¹⁵

Saudi population have better vitamin D status as compared to that in Indian Sub -continent. Naeem et al in a community based survey reported that in Saudi population of Qassim region, 28.3% population was vitamin D deficient, 39.4% was vitamin D insufficient.¹⁸ This may be explained on the basis of dietary habits as Saudi population eat a lot of cheese, sea food, mushrooms and dairy products and there is no problem of affordability which is in marked contrast to the population under study, who generally cannot afford such sources of vitamin D. Mirza J and Mohsin A in a hospital based study from Dammam, Saudi Arabia showed 98% patients with body aches to be vitamin D deficient.⁶ This can be explained on the basis of increasing trend towards obesity in Saudi population which is directly related to vitamin D deficiency.¹⁵ The only common factor Pakistani and Saudi populations had, is lack of sun exposure.¹⁴ This have been so in our population because of living in close settings, dark housings, and cultural reasons and above all lack of awareness regarding sun exposure.¹⁴ The present study revealed that almost 1/3rd of total population is having severe vitamin D deficiency and female gender was found affected more which is in agreement with what found out by Masood et al which showed

severe vitamin D deficiency in 40% of the patients especially in children, woman and elderly patients.¹⁴ This can be explained in terms of cultural practices.

The present study revealed frequency of HBsAg and anti HCV to be 12% and 18% respectively whereas Qureshi H et al in population based survey found out that prevalence of HBsAg and anti HCV to be 2.5% and 4.8 % respectively.⁷ This disparity can be explained in terms of two little sample size.

The present study also showed frequency of high blood glucose to be 16%, 3/4th of which had levels above 200 and rest had impaired glucose tolerance whereas Hakeem R and Fawwad A revealed prevalence of diabetes mellitus in Pakistan to be in the range from 7.6% to 11%. This is in agreement with what the present study noted.

CONCLUSION:

Prevalence of Vitamin D deficiency is alarming high, even more than that seen in other parts of the world. Furthermore relative frequencies of Chronic Hepatitis B, C and Diabetes mellitus are much less as compared to that of vitamin D deficiency, despite Pakistan being declared a "cirrhotic state" where Diabetes mellitus is an "epidemic".²⁸

The gravity of situation demands active efforts on the part of Government and health care providers to arrange public awareness programs highlighting the importance of sun exposure, which is the cheapest and the most abundantly available source of vitamin D. Furthermore, it is the need of the hour that practical guidelines should be established regarding vitamin D replacement in resource poor settings as ours and also that Government should ensure fortification of certain food items with vitamin D such as Ghee, bread etc.

LIMITATIONS OF THE STUDY:

Lack of resources was a major limitation to our study. Patients could not be investigated beyond anti HCV or HBsAg status for chronic hepatitis and 75 gram oral glucose tolerance test could not be ordered for patients with impaired glucose tolerance. Serum calcium, phosphate, alkaline phosphatase and parathyroid hormone levels were not done

because of the same reasons and also because of the observation that vitamin D is an independent risk factor for fatigue and does not require these investigations.¹⁶ This area requires further research. Furthermore, duration and timing of sun exposure was not recorded as almost all patients belonged to lower socio economic background, living in dark and close settings with limited sun exposure.

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The tongue of a wise man lies behind his heart.

A man's behavior is the index of his mind.

People are asleep as long as they are alive, they are awakened when they die.

Hazrat Ali
(Razi Allah Tala Anho)