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CORRELATION OF SERUM VITAMIN D LEVELS WITH SERUM LEVELS OF ALKALINE PHOSPHATASE IN PATIENTS WITH DETECTABLE HCV RNA.

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ABSTRACT… Objectives: To determine whether serum vitamin D levels are correlated with serum levels of alkaline phosphatase or not? **Study Design:** Case control cross sectional study. **Setting:** Gastroenterology unit of private teaching hospital in Peshawar. **Period:** From November 2015-Januaray 2016. **Material and Methods:** 100 participants meeting the criteria were included in the study. Fifty clinically normal young adults and fifty were non cirrhotic with detectable HCV RNA by PCR (chronic hepatitis C patients) were included in the study. Venous blood samples were taken from all the study participants and serum vitamin D levels were determined by Electro-chemiluminescence binding assay (ECLIA) and serum alkaline phosphatase was determined by Photometric Kinetics. **Results:** patients were divided into two groups on the basis of gender i.e.25 males and 25 females. A correlation between vitamin D and alkaline phosphatase was determined. Alkaline phosphatase was raised in the non cirrhotic chronic hepatitis C patients. Pearson correlation was applied to find out the relation between vitamin D levels and alkaline phosphatase in the two groups which had a significant relationship with a p-value of 0.01. A positive correlation between alkaline phosphatase and parathyroid hormone was found with a p value of <0.0001. **Conclusion:** In our study alkaline phosphate was considerably increased in chronic hepatitis C patients who might be due to underlying liver disease. In chronic liver disease the hepatocytes swell up and due to damage to the liver parenchyma the level of alkaline phosphatase increases.

Key words: Chronic hepatitis C patients, Serum vitamin D levels, Serum alkaline phosphatase.

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INTRODUCTION

Vitamin D was discovered in 1920 by Mellabany. In the time interval between 1920-1930 it was classified as a vitamin that is essential for normal development of skeleton and calcium absorption.[1,2] It is primarily produced in the skin from cholesterol derivatives.[3] The vitamin D produced in the skin is biologically inert.[4] The inactive form of vitamin D must be converted to its active form to carry out its biological functions. The active form of vitamin D i.e., 1,25 hydroxy vitamin D is produced by hydroxylation of the inactive vitamin D. It is this active form of vitamin D i.e, 25 hydroxy vitamin D that is monitored in the serum of patients to assess the status of vitamin D.[5] Vitamin D is a micro nutrient mainly produced in the skin from cholesterol precursors. The main sources of vitamin D are Liver, Beef, Eggs, Mushrooms, Milk, Dairy products, Whole grain cereal etc:[6,7]

Alkaline phosphatase is a group of identical enzymes that are natives of four homologous alkaline phosphatase genes. Three out of these four enzymes are present in different body tissues while the remaining one is present mainly in bone and liver.[7,8] The total serum alkaline phosphatase level is provided equally by bone and liver. It is a factor required for bone mineralization and synthesis of new bone. Increase serum level indicates increase bone turn over.[9] Steven R Lacey in 2014 conducted a retrospective study about the routine biochemistry in suspected vitamin D deficiency.

METHODOLOGY

A case control cross sectional study was conducted in the gastroenterology unit of hospitals attached to Peshawar medical college from November 2015-januaray 2016. A total of 100 participants meeting the criteria were included in the study. Fifty clinically normal young adults and fifty were non cirrhotic with HCV RNA detectable by PCR (chronic hepatitis C) patients were included in the study. For controls, apparently clinically normal young adults screened negative for hepatitis B and C were included and subjects diagnosed as diabetics, hypertensive, having autoimmune diseases, renal diseases, bone disorders or any other known metabolic disorders were excluded from the study. Non cirrhotic chronic hepatitis C patients without clinical and ultrasound evidence of cirrhosis were included and Chronic hepatitis C cirrhotic patients, patients of chronic hepatitis B were excluded. Venous blood samples were taken from all the study participants and serum vitamin D levels were determined by Electro-chemiluminescence binding assay (ECLIA) and serum alkaline phosphatase was determined by Photometric Kinetics.

Two sample t test also known as independent sample t test was applied for the inter group comparison of vitamin D and alkaline phosphatase levels. Pearson correlation was used to determine correlation between vitamin and alkaline phosphatase.

RESULTS

In the present study, vitamin D status of non cirrhotic chronic hepatitis C patients and apparently clinically normal healthy adults was determined. A comparison between the two groups was also made. Fifty participants were included in each group with 25 males and 25 females. A correlation between vitamin D and alkaline phosphatase was made. The age range was 18-40 $_{+}$ 6 years. The mean age was 29.68 in group A and 29.80 in group B and there was no statistically significant difference in the two groups with a p-value of > 0.05. The subjects were grouped into the following categories on the basis of serum vitamin D levels:

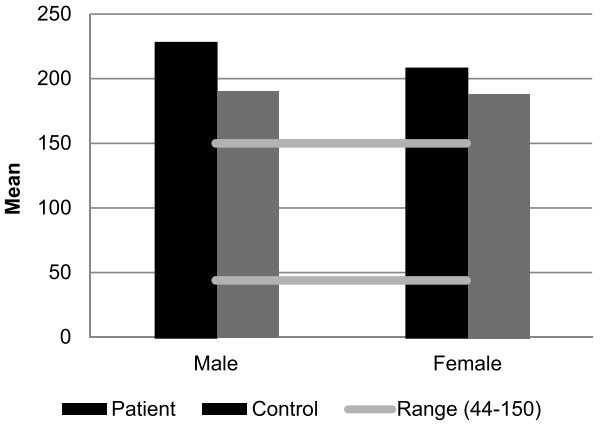
- Severe Vitamin D deficient
- Moderate Vitamin D deficient
- Normal

Among the 100 participants, 21 subjects were in the severe deficient category. Out of these 21 subjects 28.6% were from Group A and 71.4% were from Group B. This difference was statistically significant with a P-value of 0.001. Thirty three percent of the study participants had mild to moderate vitamin D deficiency. Among them 45.5% were healthy adults and 54.5% were non cirrhotic chronic hepatitis C patients. The statistical difference was not significant with p-value of > 0.05.

Forty Six percent of the study population had normal level of vitamin D. Student t-test was applied to find out the statistical difference among various variables of group A and group B. Mean of serum vitamin D in the non cirrhotic chronic hepatitis C patients was 23.16 ± 12 while it was 18.29 ± 10 in the healthy matching controls. The difference was statistically significant with a P-value of 0.02. ($p < 0.05$) Alkaline phosphatase was raised in the non cirrhotic chronic hepatitis C patients. Comparison of means of alkaline phosphatase in the two groups had a significant relationship with a p-value of 0.01. Pearson correlation was applied to find out the relation between vitamin D levels and various study variables within each group. A positive correlation between alkaline phosphatase and parathyroid hormone was found with a p value of <0.0001.[10]

Variable	Group A Mean ($\pm$ SD)	Group B Mean ($\pm$ SD)	P-Value
Vitamin D	23.32 ± 10	18.29 ± 10.4	0.02*
Alkaline phosphatise	219.06 ± 64.2	190.2 ± 32.7	0.01*

T test for the comparison of means of the different variables



Mean comparison of alkaline phosphatase values in male and females

DISCUSSION

Vitamin D deficiency is an emerging problem in Pakistan. In the present study a comparison was made between the vitamin D status of non cirrhotic chronic hepatitis C patients and healthy individuals aged between 18-40 years.

In our study fifty four percent of the total study population had vitamin D deficiency. Almost similar results were obtained from a study conducted by M. Akhtar Baig and his colleagues in Dow Medical University Karachi in 2012. In their study almost 60% of the total study population had vitamin D deficiency. Since both these studies were OPD based therefore their results showed similarity[11] However another observational study conducted in medical unit of Shifa International Hospital showed that almost 90% of the study population had some form of vitamin D deficiency.[12]

In our study 48% of the non cirrhotic chronic hepatitis C patients had some form of vitamin D deficiency. These results are similar to the study findings of Fischer et al in which they reported that 58% of patients with chronic hepatitis had vitamin D deficiency.[13] A review by Lei Yuan and co workers found that patients with chronic liver disease had a limited exposure to sunlight therefore it might be a cause of avitaminosis D in these patients.[14] However, in our study most of the participants had an adequate exposure to sunlight.

Females are usually more vitamin D deficient as compared to the males. In our study majority of the females had sub normal vitamin D levels with a P-value of < than 0.05. These findings are similar to the results of a study conducted in Kulsoom International Hospital by Haroon and his colleagues. In their study 57% of the females had vitamin D deficiency.[15]

Various metabolic parameters of both the groups have been compared with each other. It is interesting to know that vitamin D levels were considerably decreased in the normal healthy adults as compared to the non cirrhotic chronic hepatitis C patients with a (p-value 0.02). In our study alkaline phosphate was considerably increased in chronic hepatitis C patients which might be due to underlying liver disease. In chronic liver disease the hepatocytes swell up and due to damage to the liver parenchyma the level of alkaline phosphatase increases.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Farzana Salman	Abstract and recording.	
3	Mohsina Haq	Data analysis, editing.	
4	Seher Obaid	Data collection.	
5	Ambreen Gul	Drafting and analysis of samples	
6	Arbab M. Kashif khan	Approval of fianl version.