Section A-Research paper

Role of Vitamin D as one of Predictors to Outcome of vascular Portal Hypertension.

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Abstract

Background: Vitamin D role in chronic liver diseases is not well known, but there are some reports suggesting that hormone has anti-inflammatory and anti-fibrotic role, consequently, it has a significant role in the natural history of chronic liver diseases, such as chronic hepatitis C and non-alcoholic fatty liver disease (NAFLD).

Aim: Our study evaluated the correlation between vitamin D & portal hypertension and its predictive value in patients with liver cirrhosis.

Methods: This case control study was carried out on 150 patients had chronic liver disease who attended the Hepatology and endoscopy units, National Liver Institute hospitals, Menoufia University,from April 2021 to December 2021. Patient'ssubgroups were classified into: Group A (50 patients) with chronic liver disease without varices. Group B (50 patients) with CLD without bleeding varices.

Group C (50 patients) with CLD with bleeding varices. All patients were subjected to full history taking, thorough physical examination, and laboratory investigations including liver function tests, complete blood count, vitamin D, abdominal ultrasound and upper gastro esophageal endoscopy.

Results: There were difference in the mean level of vitamin D among our included groups (cirrhosis without varices vs cirrhosis with non-bleeding varices vs cirrhosis with bleeding varices (19.51 vs 17.82 vs 15.29ng/ml) but not statistically significant ($p>0.05$). In cirrhosis with bleeding varices group, there was significant positive correlation between serum vitamin D level &Albuminwhile in both non- bleeding vs bleeding groups there were significant negative correlation between serum vitamin D level and direct bilirubin, total bilirubin, PT as well as INR.

Conclusion: We found difference in the mean level of vitamin D among our included groups but not statistically significant. Moreover, we did not find vitamin D as predictor for bleeding varices.

Key words: Vitamin D;Predictors; Portal hypertension.

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1. Introduction

Vitamin D is a fat-soluble and steroid hormone with a pleiotropic effect on human health and many chronic diseases. It is necessary for functions and health of bothmuscles and bones in our body. Also, vitamin D hasmany extra skeletal functions. Many chronic diseases, likediabetes mellitus, chronic infections and malignancy (breast ,prostate and colon), are less likely to develop with presence ofadequate stores of vitamin D in our body because many cells ofthe body like hepatocytes, macrophages, immune B and T cellsexpress vitamin D receptors on their surface **(1)**.Patients suffering from chronic liver diseases are mostly vitamin D deficient. It is estimated about one-third of cirrhotic patients havevitamin D deficiency **(2).**

Different factors can explain vitamin D deficiency inACLD. Patients affected by acute on chronic liver disease (ACLD) have reduced exposure to vitamin D sources throughlow sunlight exposure and malnutrition; moreover, there is a low intestinal hormoneabsorption and a

decreased production of binding proteins (DBP and albumin), which are Responsible for transferring vitamin D to the liver and kidney so it can be activated. Lastly **,**a non-effective hydroxylation of vitamin D leads to lower levels of active hormones, whilethe catabolism of the vitamin is increased **(3).**

Vitamin D deficiency is common in chronic liver disease (CLD) patients .up to 93% of these patients have some degree of vitamin D insufficiency .even patients with mild liver disease are also affected ,liver cirrhosis patients more commonly suffer from severe deficiency **(4).**

Many studies have shown that low levels of 25(OH) D significantly increase the risk of mortality from all causes, including cardiovascular diseases **(5).**

The aim of this work wasassessment of the role of Vitamin D as one of predictors to outcome of portal hypertension especially varices and their sequale.

2. Patients and Methods

This case control study was carried out on 150 patients with liver cirrhosis who were recruited from hepatology and endoscopy units, National Liver Institute, Menoufia University, starting from April 2021 to December 2021. Adults age older than 18 years of age of both sexes who had established diagnosis of liver cirrhosis of any etiology attending hepatology and endoscopy unit for upper gastrointestinal endoscopy were included in the study after an approval from the ethical committee of the National liver Institute, Menoufia University along with patients' written informed consent were prerequisites before commencing the study IRB (00000).

Patients were classified into three groups:

-**Group A**: 50 patient's liver cirrhosis patients without esophageal varices.

-**Group B**: 50 patient's liver cirrhosis patients with non-bleeding esophageal varices.

-**Group C**: 50 patient's liver cirrhosis patients with bleeding esophageal varices.

Serum vitamin D (25 hydroxy vitamin D) about 2mlof blood was collected from each patient and respective attendant in dark room. Serum was separated from the blood and preserved at -20 c for estimation of vitamin D levels. Patients were categorized on the basis of serum vitamin D (25-OHD) level deficiency < 20 ng/ml, insufficiency 20–29.9 ng/ml, sufficiency 30–100 ng/ml, and potential toxicity >100 ng/ml, **Upper esphago-gastric endoscopy:** for detection of esophageal varices and bleeding. Data was collected, coded then entered as a spread sheet using Microsoft Excel 2016 for Windows, of the Microsoft Office bundle; 2016 of Microsoft Corporation, United States. Data was analyzed using IBM Statistical Package for Social Sciences software (SPSS), (IBM SPSS Statistics for Windows, and Version 26.0. Armonk, NY: IBM Corp). The Kolmogorov-Smirnov test was used to verify the normality of distribution. Continuous data was expressed as mean ± standard deviation, median & IQR while categorical data as numbers and percentage. A statistical value <0.05 was considered as significant.

3. Results

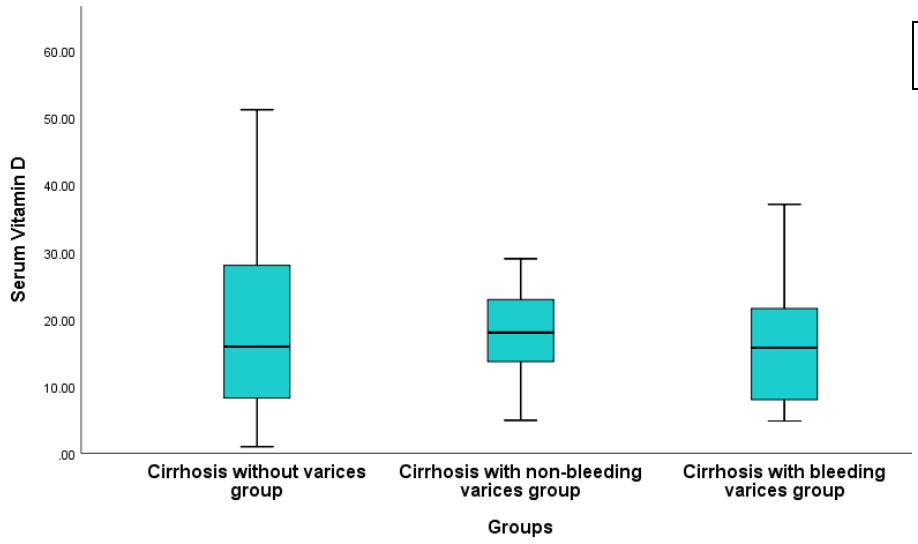
The mean level of serum vitamin D in cirrhosis without varices group was 19.51± 13.18, 17.82± 7.09 in cirrhosis with non-bleeding varices group and 15.29± 8.51 in cirrhosis without varices group. There was no statistically significant difference between the three studied groups regarding serum vitamin D level (p>0.05) **Table (1)**.

In cirrhosis with non-bleeding varices group, there was significant positive correlation between serum vitamin D level and ALT while there was significant negative correlation between serum vitamin D level and direct bilirubin, total bilirubin, PT as well as INR. **In cirrhosis with bleeding varices group**, there was positive correlation between serum vitamin D and Albumin while there was significant negative correlation between serum vitamin D level and direct bilirubin, and total bilirubin, INR, PT **Table (2).**

Table (1): Comparison between the studied groups regarding serum vitamin D level.

Serum vitamin D level	Cirrhosis without varices group (n.= 50)	Cirrhosis with non-bleeding varices group (n.= 50)	Cirrhosis with bleeding varices group (n.= 50)	P-value
Mean± SD	19.51± 13.18	17.82± 7.09	15.29± 8.51	0.165

p≤0.05 is considered statistically significant, p≤0.01 is considered highly statistically significant,SD: standard deviation, analysis done by X^2: Chi-Square Test& KW: Kruskal-Wallis Test.

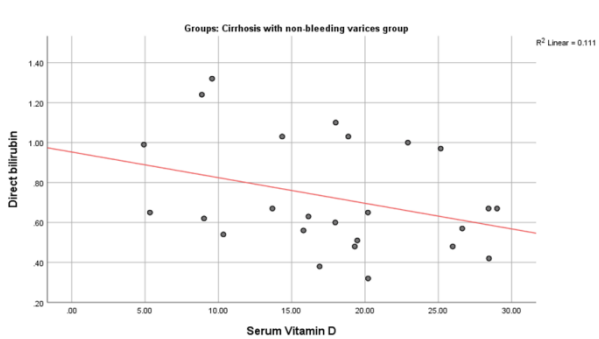


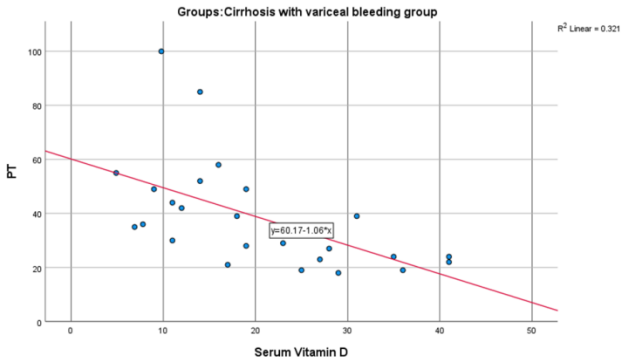
p-value >0.05

Difference between the study groups regardingserum vitamin D level.

Table (2): Correlation between serum vitamin D level and different parameters in the three studied groups.

	Cirrhosis without varices group (n.= 50)		**Cirrhosis with non-bleeding varices group (n.= 50)**		**Cirrhosis with bleeding varices group (n.= 50)**	
	Serum vitamin D level					
	R	**p-value**	**R**	**p- value**	**r**	**p- value**
Spleen size	-.185-	0.219	-.015-	0.920	-.248-	.082
Liver size	.073	0.616	.195	0.175	.120	.406
Albumin	.132	0.361	.060	0.680	.329	**.020**
Direct bilirubin	-.132-	0.361	-.304-	**0.032**	-.312-	**.014**
Total bilirubin	-.145-	0.315	-.297-	**0.036**	-.301-	**.021**
ALT	-.247-	0.084	.369	**0.008**	-.041-	.778
AST	-.189-	0.188	.271	0.057	-.016-	.911
PT	-.220-	0.124	-.303-	**0.033**	-.285-	**.045**
INR	-.329-	0.652	-.348-	**0.020**	-.065-	**.013**
HB	-.233-	0.104	-.033-	0.819	.013	.929
WBCS	-.005-	0.972	.033	0.821	.020	.892
Platelet count	.065	0.652	.098	0.498	.000	.998
Platelet count to spleen diameter ratio	0.237	0.113	.101	0.495	.009	.951





1. Scatter plot showing negative correlation between serum vitamin D level and direct bilirubin in cirrhosis with non-bleeding varices group.
2. Scatter plot showing negative correlation between serum vitamin D level and PT in cirrhosis with bleeding varices group.

4. Discussion

We found that up to 92% of patients with liver cirrhosis suffer from Vitamin D deficiency when taking >30 ng/ml as normal level, whereas 64% where found deficient when taking <20 ng/ml as the cut-off. These results are in line with the literature when 20 ng/ml was taken as a cut-off; **Stokes et al(3)** reported that 86% of cirrhotic patients were deficient and another study performed in Austria by **Putz-Bankuti et al(6)**found 71% deficient (<20 ng/ml) patients so the real number might be somewhere around 80%. Those results also fit the literature for patients with chronic liver disease (CLD) where Lange et al found 66% of chronic HCV patients in a deficient state.

Our results showed that there were difference in the mean level of vitamin D among our included groups (cirrhosis without varices 19.51, cirrhosis with non-bleeding varices 17.82, and cirrhosis with bleeding varices 15.29) but not statistically significant (p>0.05) in accordance with **Jamil Z et al. (7)** and in contrast to the study **Zhao M Y et al. (8)** which conducted on 83 patients 51 bleeding group & 32 non bleeding group with p value 0.002.

Regarding the level of vitamin D there was no statistically difference between the studied three groups in contrast to this study **Zhao M Y et al. (8).**

As regard vitamin D level we found that In cirrhosis with bleeding varices group, there was significant positive correlation between serum vitamin D level and Albumin(r .329 ,p= .020) while in both non- bleeding and bleeding groups there were significant negative correlation between serum vitamin D level and direct bilirubin (r-.304- , p=.032and r-.312-, p=.014 respectively) , total bilirubin(r -.297-,p =.036and r-.301-,p=.020 respectively) , PT (r -.303- ,p=.033and r-.285-,p=.045 respectively)as well as INR (r -.348-,p=.020 and r -.065-,p=.013 respectively) in accordance with **Jamil Z et al. (7)** for (Albumin), **Paternosto et al (9)** for (Albumin and PT) and **Khan et al (4)** for (Albumin and bilirubin).

5. Conclusion

We found difference in the mean level of vitamin D among our included groups (cirrhosis without varices 19.51, cirrhosis with non-bleeding varices 17.82, and cirrhosis with bleeding varices 15.29) but not statistically significant. Moreover, we did not find vitamin D as predictor for bleeding varices.

6. Acknowledgements

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7. Disclosure

The authors declare no conflict of interest.

8. References

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