LIVER CIRRHOSIS ON HISTOMORPHOLOGY AND VITAMIN D DEFICIENCY: A CROSS-SECTIONAL STUDY AT TERTIARY CARE HOSPITAL OF PESHAWAR, PAKISTAN

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ABSTRACT

Objectives: *To estimate the frequency of vitamin D insufficiency in individuals with cirrhosis of the liver based on histomorphology.*

Methods and materials: *In the current investigation, 148 patients were tracked to determine the incidence of vitamin D insufficiency in adults with liver cirrhosis based on histomorphology. All those participants, both males and females, with liver cirrhosis (of any severity) for at least 06 months and aged 30 to 60 years were included whereas, the individuals with osteomalacia or vitamin D insufficiency (as determined by medical records) and chronic renal failure (as determined by specific investigations or medical records) were excluded in the study.All patients presenting to OPD meeting the inclusion criteria i.e. people with cirrhosis. Vitamin D insufficiency was stratified by age, gender, and disease duration to examine the impact modifiers using the chi square test having a p-value of <0.05 regarded as noteworthy by Using SPSS version 20.*

Results: *In the present study, the age distribution of 148 patients was examined which was; from 30-40 years were 41 (27.7%), 41-50 years were 60 (40.5%) and from 51-60 years were 47(31.8%). Average age was 55.56±3.357 years. Gender wise distribution among 148 patients was analysed as; males were 94 (63.5%) and females were 54 (36.5%). Distribution of BMI classification among 148 patients was analysed as; below 18.5 (underweight) was 60 (40.5%), 18.5-24.9 (normal weight) were 43 (29.1%), 25.0-29.9 (pre-obesity) were 19 (12.8%) and 30.0-34.9 (obesity class) were 26 (17.6%). Distribution of diabetes among 148 patients were analysed as; Yes was found in 57 (38.5%) and No was found in 91 (61.5%). Distribution of smoking among 148 patients were analyzed as; Yes, was found in 51 (34.5%) whereas No was found in 97(65.5%).*

Conclusion: *The link between vitamin D and liver cirrhosis on histomorphology has significant therapeutic promise. We expect to look into a variety of extra-skeletal indications in the near future. The link between vitamin D deficit and liver function, infectious effects, and fibrosis may back its use as a prognostic as well as suggestive tool.*

Key words: *Diabetes, histomorphology, liver cirrhosis, smoking, vitamin d deficiency*

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INTRODUCTION

Liver cirrhosis manifests itself histologically as regenerating nodules surrounded by fibrous bands, resulting in portal end-stage liver disease and hy-

pertension[1]. Although Cirrhosis globally prevalent at unknown scale, yet it is assumed to be approximately 1%[1,2]. A significant number of cases remain unidentified, and it is still often discovered through autopsies[3]. Cirrhosis is most commonly caused by chronic viral hepatitis, excessive alcohol addiction, and non-alcoholic fatty liver ailment with geographical variations. According to research, hepatitis is the leading cause of cirrhosis in Pakistan, with hepatitis c virus (HCV) accounting for 41%-52% of the cases, preceded by hepatitis b virus (HBV) accounting for 30% of cases[4,5]. Vitamin-D belongs to a seco-steroid hormone that is best recognized as regulators of the metabolism of calcium and bone. Vitamin D, on the other hand, has pleiotropic properties such as cellular propagation, differentiation, and immunomodulation[6]. These extra-skeletal activities are linked to the development as well as therapy of contagions, deteriorating, autoimmune, and cardiovascular illnesses, as well as a variety of cancer types. Although studies claim that this hormone has anti-inflammatory and anti-fibrotic actions, and thus plays a key part in medical record of chronic liver disorders including long-term hepatitis C and non-alcoholic fatty liver ailments, significance of vitamin D in ongoing liver illnesses is unknown[7,8]. Vitamin D insufficiency is caused by a number of ways[9]. Reduced vitamin D levels in chronic liver disorders are linked to malnutrition as well as a lack of sunshine exposure. Furthermore, decreased intestinal absorption of vitamin D has been associated to liver disease and is also characterised by modest amounts of attachment proteins (dbp and albumin) that can transport the hormone to trigger in the liver and kidney. Furthermore, hepatic hydroxylation of vitamin D is inhibited, resulting in small active hormone creation, whereas vitamin catabolism is increased[10]. According to one study, 46 percent of the normal population had a 25(oh) D deficiency, 51.85 percent of cirrhotic patients had a deficiency, and 28.12 percent had an insufficiency[11]. Another study found that cirrhotic people have an 88 percent and a 43 percent frequency of vitamin D deficiency[12,13]. Globally, it is estimated that 3% of people are infected with the hepatitis C virus, implying that the 170 million carriers are at risk of developing liver cancer or cirrhosis[12]. The current investigation aims to estimate the prevalence of vitamin D deficiency in people having liver cirrhosis. As previously said, vitamin D insufficiency is a global issue that is currently adding more to the global burden of chronic illnesses. Moreover, local statistics are rare and the results from literature reflect that vitamin D deficiency in cirrhotic patients varies from one population to another and this requires regular fresh evidence of the deficiency in local cirrhotic population. This study provides present local data on the scale of the problem, and the findings work as local evidence and a gateway for subsequent researches, with suggestions for prevention and management produced afterwards. Thus, the aim of this study was to determine the frequency of vitamin D insufficiency in individuals with liver cirrhosis based on histomorphology.

MATERIALS AND METHODS

This was a descriptive cross-sectional study performed at the Department of Gastroenterology at Hayatabad Medical Complex, Peshawar, Pakistan. Having ethically approved from Institutional Ethical Review Board (IERB) of Nowshera Medical College, Nowshera, Pakistan, vide its letter No: 26/NMC/IERB/Sec dated 15/09/2020. This research was carried out between the 1st of October, 2020 and the 31st of March, 2021. The size of sample was estimated utilizing the WHO algorithm for the calculation of size of sample by 43 percent[13], the prevalence of vitamin D insufficiency in liver cirrhosis, 95 percent as confidence interval with margin of error of 8 percent, and a p-value of 0.05 regarded as significant. For analysis of data, the non-probability consecutive sampling method was employed. All those participants, both males and females, with liver cirrhosis (of any severity) for at least 06 months and aged 30 to 60 years were included whereas, the individuals with osteomalacia or vitamin D insufficiency (as determined by medical records) and chronic renal failure (as determined by specific investigations or medical records) were excluded in the study.All patients presenting to OPD meeting the inclusion criteria i.e. people with cirrhosis. After describing the aim and advantages of the trial, all patients provided written informed permission. At the time of admission, 10cc of blood was drawn from each patient and immediately submitted to the hospital laboratory to be tested for vitamin D insufficiency. All investigations were submitted to the hospital laboratory, where they were completed by a single competent pathologist with at least five years of experience. All data was entered into an

organized specimen. Criteria of exclusion were rigorously followed to manage the confounding variables and bias.SPSS version 20 was used as data analysis software application to analyse the data. For quantitative variables such as age, BMI, serum vitamin D level, and duration of disease, mean and standard deviation were computed, whereas frequency/percentages were measured for independent variables such as smoking, diabetes, gender, and vitamin D insufficiency. Vitamin D insufficiency was stratified by age, gender, and disease duration to examine the impact modifiers using the chi square test having a p-value of <0.05 regarded as noteworthy..

RESULT

TThe current study, age distribution of 148 patients was examined which was; from 30-40 years were 41 (27.7%), 41-50 years were 60 (40.5%) and from 51-60 years were 47 (31.8%). Average age was 55.56±3.357 years. Gender wise distribution among 148 patients was analysed as; males were 94 (63.5%) and females were 54 (36.5%). Distribution of BMI classification among 148 patients was analysed as; below 18.5 (underweight) was 60 (40.5%), 18.5-24.9 (normal weight) were 43 (29.1%), 25.0-29.9 (pre-obesity) were 19 (12.8%) and 30.0-34.9 (obesity class) were 26 (17.6%). Distribution of diabetes among 148 patients were analysed as; Yes was found in 57 (38.5%) and No was found in 91 (61.5%). Distribution of smoking among 148 patients were analysed as; Yes was found in 51 (34.5%) whereas No was found in 97 (65.5%). Distribution of Vitamin D deficiency among 148 patients were analysed as; Yes was found in 66 (44.6%) whereas No was found in 82 (55.4%) individuals. Stratification of Vitamin D deficiency with respect to BMI, duration of disease, diabetes and smoking in given in Tables 1-4.

DISCUSSION

In the present study, the age distribution of 148 patients was examined which was; from 30-40 years were 41 (27.7%), 41-50 years were 60 (40.5%) and from 51-60 years were 47 (31.8%). Average age was 55.56±3.357 years. Gender wise distribution among 148 patients was analysed as; males were 94 (63.5%) and females were 54 (36.5%). Distribution of BMI classification among 148 patients was analysed as; below 18.5 (underweight) was 60 (40.5%), 18.5-24.9 (normal weight) were 43 (29.1%), 25.0-29.9 (pre-obesity) were 19 (12.8%) and 30.0-34.9 (obesity class) were 26 (17.6%). Distribution of diabetes among 148 patients were analyzed as; Yes, was found in 57 (38.5%) and No was found in 91 (61.5%). Distribution of smoking among 148 patients were analyzed as; Yes, was found in 51 (34.5%) whereas No was found in 97 (65.5%). Distribution of Vitamin D deficiency among 148 patients were analyzed as;

Table 2: Stratification of Vitamin D deficiency with respect to duration of disease (n=148)

Vitamin D Deficiency	Duration of Disease		Total	P-value
	6 Months	More than 6 Months		
Yes	66	0	66	0.0000
No	0	82	82	
Total	66	82	148	

Table 1: Stratification of Vitamin D deficiency with respect to BMI (n=148)

Vitamin D Deficiency	BMI				Total	P-value
	Below 18.5 Underweight	18.5–24.9 Normal weight	25.0–29.9 Pre-obesity	30.0–34.9 Obesity class		
Yes	41	0	0	25	66	0.0000
No	19	43	19	01	82	
Total	60	43	19	26	148	

Table 3: Stratification of Vitamin D deficiency with respect to diabetes (n=148)

Vitamin D Deficiency	Diabetes		Total	P-value
	Yes	No		
Yes	57	09	66	0.0001
No	0	82	82	
Total	57	91	148	

Table 4: Stratification of Vitamin D deficiency with respect to smoking (n=148)

Vitamin D Deficiency	Smoking		Total	P-value
	Yes	No		
Yes	51	15	66	0.0001
No	0	82	82	
Total	51	97	148	

Yes, was found in 66(44.6%) whereas No was found in 82 (55.4%) individuals.

Vitamin D is playing an increasingly important role in invulnerability, cancer, contagious ailments, fibrosis, and chronic liver disease. The literature has thoroughly investigated the pleiotropic properties of this hormone, including the directive of more than 200 genes involved in cell proliferation and differentiation, immune-modulation, inflammation, and fibrogenesis, as well as its effect on liver disease. Ramachandran V et al.[14] proposed two distinct pools of 1, 25(OH) 2D3 for various applications. The primary pool, which contains the conventional liver-kidney loop, increases intestinal calcium captivation and transfers active calcium (calbindin) through the intestinal mucosa via action mediation, which keeps blood calcium homeostasis and permits calcium deposition for bone formation. The another pool comprises the immune system and the local calcitriol creation by immune cells (monocytes, macrophages, dendritic cells, B and T cells, and lymphocytes) that may aid in immune system working (having the potential to defend against infections)[14]. These different pools may contribute to two unique homeostatic roles, basically endocrine and paracrine, however this is not well understood.

Guy S et al. defined our present knowledge of vitamin D pathophysiology in relation to liver cirrhosis as a complicated interaction between liver impairment, vitamin D, and familial factors of vitamin D insufficiency[15]. A number of investigations on cirrhotic individuals corroborate the frequency of vitamin D inefficiency in the present populace. The question of whether liver injury causes disruptions in vitamin D homeostasis or the other means around remains unanswered, creating a sort of chicken or egg causation quandary. Regardless of its involvement in liver cirrhosis, vitamin D certainly evaluated as an indicative tool and prognostic marker. There is growing evidence that vitamin D status has a substantial impact on health in the overall population as well as in those with chronic liver illnesses, cirrhosis, and hepatocellular carcinoma. Moreover, the association between low vitamin D levels and liver inadequacy and contagions supports vitamin D's use as a prognostic indicator in the cirrhotic populace[15]. The effectiveness of vitamin D subjunction on SVR in persons with chronic hepatitis C undergoing interferon-based therapy is currently being questioned. This has to be clarified because the majority of published research involved individuals with normal liver function and mild fibrosis. However, when a direct acting antiviral medication was used, vitamin D supplementation for higher SVR rates is anticipated to diminish along with interferon usage[15].

The problem of vitamin D sub junction for bone loss in liver cirrhosis and cholestatic ailments is covered in current clinical recommendations. Some argue, however, that the recognised criteria for vitamin D deficiency and deficiency may not apply to cirrhotic people. It is important to address the specifics of vitamin D sub junction including the starting point for subjunction, optimum period, various extra-skeletal symptoms relating to the liver, dosage modification, route of administration and bioavailability, pre-handling screening pauses, and treatment effectiveness/observation. Furthermore, there are issues about the accurateness of the various 25(OH) D investigations that must be talked.

CONCLUSION

Consequently, there was a substantial therapeutic association between vitamin D and liver cirrhosis on histomorphology. A variation of extra-skeletal signals is expected to be investigated further in the near future. The link between vitamin D shortage and liver function, fibrosis, and contagious effects may warrant its use as a predictive and diagnostic tool. To properly analyse and validate the effect of vitamin D in liver cirrhosis, large potential cohort studies and randomised trials are required.

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