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Original Research Article

An Assessment of Serum Vitamin-D Level among Adult Non-Alcoholic Fatty Liver Disease Patients: A Study in a Tertiary Care Hospital in Eastern Odisha

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Conflict of interest: Nil

Abstract:

Background: Non-alcoholic fatty liver disease (NAFLD) has become a global epidemic. Approximately every third adult in the industrialized countries has a morbidly fatty liver. NAFLD is the most common cause of persistent abnormalities in liver enzymes. NAFLD is now increasingly being recognized as a cause of hepatocellular carcinoma, liver transplantation and finally death. Vitamin D, the sunshine vitamin, can be associated with the progression of NAFLD. Many studies have shown a correlation between Vitamin D and NAFLD.

Materials and Methods: 50 cases and 50 controls were selected for the study over an approximate period of 2 years. The study was a cross-sectional study done in IMS & SUM Hospital

Results: The difference of mean Vitamin D level was found to be statistically significant between the cases and the controls. Alanine Transaminase level was also found to be statistically significant.

Conclusion: Our study revealed that lower Vitamin D levels were found in patients suffering from NAFLD. However more studies are required to concretely establish this finding.

Keywords: NAFLD, liver disease, alcohol, Vitamin D, sunshine vitamin, cirrhosis, NASH.

Introduction

Non-alcoholic fatty liver disease (NAFLD) involves fatty infiltration of the liver exceeding 5% to 10% by weight with exclusion of alcohol as a cause [1]. It was described for the first time in 1950 when fatty liver was observed in a group of obese patients.[2]

The prevalence of NAFLD is increasing rapidly worldwide. In western countries, NAFLD is the most common liver disorder, and it has a reported prevalence of 6-35% (median 20%) worldwide. NAFLD among Adult population is about 25-30% and non-alcoholic steatohepatitis (NASH) prevalence in adults is about 5-6% [3, 4].

However, in Indian population prevalence rate of NAFLD is increasing day by day. In the general Indian population prevalence of the disease is reported to be around 8.7-32%, with a higher incidence rate observed among obese and diabetic patients depending on age, gender, locality and ethnicity [5,6-10]. Prolonged use of medicines like amiodarone, Antiviral drugs (nucleoside analogues), corticosteroids, methotrexate, tamoxifen, tetracycline, etc can be attributed as one of the causes of NAFLD.[11]

Cigarette smoking is not associated with an increased risk of developing NASH but some studies showed that consumption of large quantities of soft drinks can cause NAFLD due to high concentrations of fructose - corn syrup or in similar quantities, as a metabolite of sucrose. The quantity of fructose delivered by soft drinks may lead to increased deposition of fat in the abdomen.[12,13]

Lipid disorders associated with metabolic syndrome (like hypertriglyceridemia rather than hypercholesterolemia) may trigger the risk of NAFLD [10,14]. The progression from NAFLD to NASH and cirrhosis is less understood but increasing evidence suggests that the mechanism

of the association of vitamin D and NAFLD is believed to be related to oxidative stress and inflammation.[15] They both share inflammation as the common pathogenic mechanism. Several researchers in the last two decades have already examined the correlation between NAFLD and vitamin-D level.[1,16-22]

Gradual weight loss may improve the process in obese NAFLD patients; rapid loss may worsen disease progression. [23]

Materials and Methods

50 known cases of NAFLD (aged between 18-70 years and with history of alcohol intake ≤30g/day in men and ≤ 20g/day in women), presented to the Gastroenterology Department, Institute of Medical Sciences & SUM Hospital during the period of 2016-2017were included as cases in my study. Pregnant women and those having other chronic diseases, any malignancies or taking vitamin D supplementation were excluded. The diagnosis of NAFLD was made on the basis of ultrasonography findings.

Subjects were considered as cases if they presented with fatty liver defined according to the standard criteria accepted by the American Gastroenterology Association.[24] The standard criteria are:- An increase in hepatic echogenicity taking renal echogenicity as a reference, the presence of enhancement and lack of differentiation in periportal intensity and the vascular wall due to great hyperechogenicity of the parenchyma.[25]

Calculated Parameters:

1. Very-low density lipoprotein (VLDL-c) estimation done by Friedewald's equation: (Triglycerides/5).
2. Low-density lipoprotein cholesterol (LDL-c) estimation done by following formula: [Total cholesterol – (HDL+VLDL)].
3. Globulin = [Total protein – albumin].
4. A : G ratio
5. Lipid ratios

Results & Discussion

In the present study 50 cases of non-alcoholic fatty liver disease (NAFLD) were compared with 50 nos. of age and sex matched healthy controls by using software SPSS version 20.0.

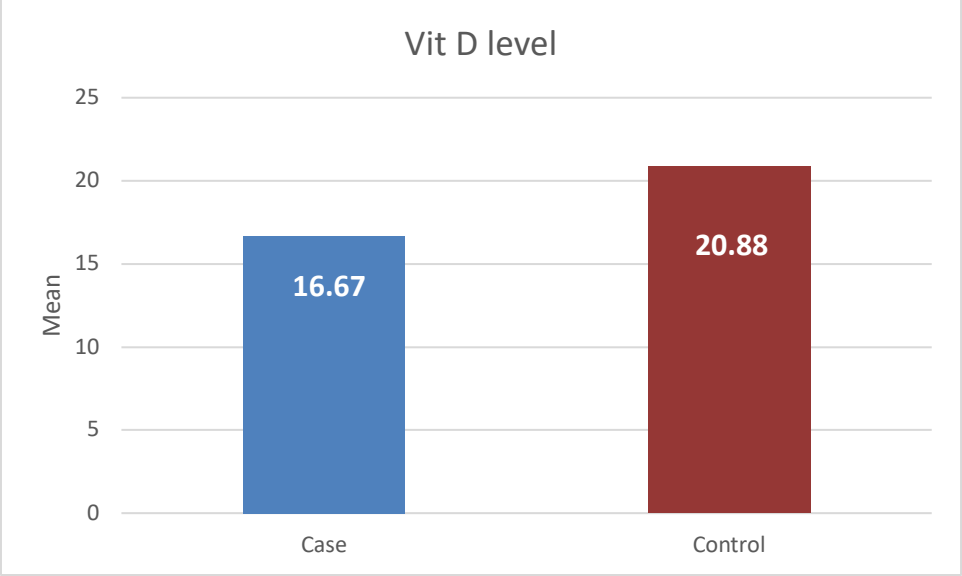

Figure 1: Mean values of vitamin D in both the groups

Table 1: Comparison of Vitamin D Level between the Groups.

Parameters	Cases (Mean ± SD)	Control (Mean ± SD)	P value*
Vitamin D	16.67 ± 8.72	20.88 ± 9.46	**0.027**

*Mann-Whitney U test was used.

Table 1 and figure 1 show the comparison of Vitamin D level in between the groups. The mean Vitamin D level in patient with NAFLD was 16.67 ± 8.72 which was lower than the control group.

This Vitamin-D level when compared between the 2 groups, using a Mann- Whitney U test was found to be statistically significant (p value= 0.027).

Previously, many studies have reported that the serum vitamin D levels of the patients with NAFLD/NASH were lower than those without diseases, suggesting that NAFLD might cause vitamin D deficiency in these patients. As a secosteroid associated with calcium homeostasis, the functions of Vitamin-D on immune modulation, cell differentiation and proliferation,

and the inflammatory response have already be confirmed. [26] For instance, Vitamin-D deficiency would activate Toll-like receptors, resulting in severe liver inflammation and induction of oxidative stress. Vitamin-D supplements could reverse the inflammation caused by NAFLD-related hepatic injury by inhibiting monocyte activation and TNF-α and IL-1 expression. [27,28] So, a strong association of circulating low vitamin-D level in NAFLD patients was an important finding of the present study. In contrast, some studies analyzed by Brilet al.[29], Hao et al.[30], Eun Chung et al.[31] and Li et al.[32] did not find any significant correlation in between adult NAFLD cases compared with control group.

Table 2:

Parameters	Cases (Mean ± SD)	Control (Mean ± SD)	P value*
TG	168.0 ± 48.9	137.90 ± 55.74	**0.001**
HDL	43.88 ± 9.58	47.50 ± 13.89	0.393
LDL	93.0 ± 38.0	91.5 ± 30.60	0.951
VLDL	32.28 ± 11.65	26.46 ± 12.22	**0.002**
Total Cholesterol	174.35 ± 36.77	170.42 ± 31.81	0.837

*Mann-Whitney U test was used.

Table 2 shows the comparison of lipid profile in between the groups. Triglyceride levels in case group (168.0 ± 48.9) was found to be higher as compared to control group (137.90 ± 55.74) and it is statistically significant (p value= 0.001). Similarly, VLDL levels were significantly higher in case group (32.28 ± 11.65) as compared with control group (26.46 ± 12.22) (p value= 0.001).

Table 3: Comparison of Liver Function Test between the Groups

Parameters	Cases (Mean ± SD)	Control (Mean ± SD)	P value*
AST	29.84 ± 14.10	28.16 ± 15.45	0.465
ALT	38.24 ± 24.41	26.56 ± 16.41	**0.001**
ALP	96.62 ± 36.41	83.44 ± 20.27	**0.040**

Mildly to moderately elevated serum levels of ALT and/or AST is the most common laboratory abnormality found in patients with NAFLD. Specially, ALT concentrations are sometimes used as a biomarker to detect "suspected NAFLD". [36,37]

Table 4: Comparison of Protein Levels between the Groups.

Parameters	Cases (Mean ± SD)	Control (Mean ± SD)	P value*
Albumin	3.86 ± 0.890	4.08 ± 0.488	0.125
Globulin	3.08 ± 1.02	2.96 ± 0.699	0.496
Total Protein	6.98 ± 1.33	6.98 ± 0.685	0.998
A: G Ratio	1.33 ± 0.48	1.51 ± 0.653	0.129

*Unpaired t-test was used.

Table 4 shows the comparison of protein levels between the groups. The mean albumin level in the NAFLD patients was 3.86 ± 0.890 whereas the albumin level was 4.08 ± 0.488 in control group. The difference did not show any statistical significance (p value= 0.125).

The comparison of mean globulin level, total protein level and A:G ratio between the two groups did not show any statistical significance

Summary and Conclusion

The present cross-sectional study was conducted on 50 patients with non-alcoholic fatty liver disease (NAFLD) and compared with 50 healthy participants in a tertiary care hospital.

From the current study, it can be concluded that the serum level of vitamin-D among adult NAFLD patients were lower than adult healthy individuals.

An attempt has been made to explain the lowering level of serum vitamin-D in non-alcoholic fatty liver disease patients and its role in disease progression.

However, further studies with larger case population and longer time frame are required to explain the central pathophysiology in non-alcoholic fatty liver disease progression.

References

1. Zakim and Boyer's hepatology: a text book of liver disease/[edited by] Thomas D. Boyer, Michael P. Manns, Arun J.sanyal. 6th ed. ISBN 978-1-4377-0881-3
2. Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson J, Loscalzo J. eds. Harrison's Principles of Internal Medicine, 18e. New York, NY: McGraw-Hill; 2012.

3. Bedogni G, Miglioli L, Masutti F, et al. Incidence and natural course of fatty liver in the general population: the Dionysos study. Hepatology. 2007; 46:1387–1391.
4. S. Bellentani, F. Scaglioni, M. Marino, and G. Bedogni, "Epidemiology of nonalcoholic fatty liver disease," Digestive Diseases, 2010; 28(1): 155–161.
5. Mohan V, Farooq S, Deepa M, Ravikumar R, Pitchumoni CS. Prevalence of nonalcoholic fatty liver disease in urban South Indians in relation to different grades of glucose intolerance and metabolic syndrome. Diabetes Res Clin Pract 2009; 84:84-91.
6. Amarapurkar D, Kamani P, Patel N, Gupte P, Kumar P, Agal S, et al. Prevalence of non-alcoholic fatty liver disease: Population based study. Ann Hepatol 2007; 6:161-3.
7. Das K, Das K, Mukherjee PS, Ghosh A, Ghosh S, Mridha AR, et al. Nonobese population in a developing country has a high prevalence of nonalcoholic fatty liver and significant liver disease. Hepatology 2010; 51:1593-602.
8. Singh SP, Nayak S, Swain M, Rout N, Mallik RN, Agrawal O, et al. Prevalence of nonalcoholic fatty liver disease in coastal eastern India: A preliminary ultrasonographic survey. Trop Gastroenterol 2004; 25:76-9.
9. Bajaj S, Nigam A, Luthra A, Pandey RM, Kondal D, Bhatt SP, et al. A case-control study on insulin resistance, metabolic co-variates & prediction score in non-alcoholic fatty liver disease. Indian J Med Res 2009; 129:285-92.
10. Majumdar, P. Misra, S. Sharma, S. Kant, A. Krishnan, and C. S. Pandav, "Prevalence of nonalcoholic fatty liver disease in an adult population in a rural community of Haryana, India," Indian Journal of Public Health, 2016;60(1): 26–33.
11. Adams LA, Angulo P. "Treatment of non-alcoholic fatty liver disease". Postgrad Med J. 2006;82 (967): 315–22.
12. Nseir, W.; Nassar, F.; Assy, N. "Soft drinks consumption and nonalcoholic fatty liver disease". World Journal of Gastroenterology. 2010;16 (21): 2579-2588.
13. Allocca, M; Selmi C. "Emerging Nutritional treatments for nonalcoholic fatty liver disease". In Preedy VR; Lakshman R; Rajaskanthan RS. Nutrition, diet therapy, and the liver. CRC Press. 2010; 131–146. ISBN 1420085492.
14. Close GL, Russel J, Coblet JN, Owens DJ, Wilson G, Gregson W, Fraser WD, Morton JP. Assessment of vitamin D concentration in non-supplemented professional athletes and healthy adults during the winter months in the UK: implications for skeletal muscle function. J. Sports Sci. 2013;31(4):344-353.
15. Ratziu V, Charlotte F, Heurtier A, Gombert S, Giral P, Bruckert E, Grimaldi A, Capron F, Poynard T. Sampling variability of liver biopsy in nonalcoholic fatty liver disease. Gastroenterology 2005;128:1898-906.
16. Manco M, Ciampalini P, Nobili V. Low levels of 25-hydroxyvitamin D(3) in children with biopsy-provennon alcoholic fatty liver disease. Hepatology. 2010; 51: 2229.
17. Nakano T, Cheng YF, Lai CY, Hsu LW, Chang YC, et al. Impact of artificial sunlight therapy on the progress of non-alcoholic fatty liver disease in rats. J Hepatol. 2011; 55: 415-425.
18. Roth CL, Elfers CT, Figlewicz DP, Melhorn SJ, Morton GJ, et al. Vitamin D deficiency in obese rats exacerbates nonalcoholic fatty liver disease and increases hepatic resist in and toll-like receptor activation. Hepatology. 2012; 55: 1103-1111.
19. Barchetta I, Angelico F, Del Ben M, Baroni MG, Pozzilli P, et al. Strong association between non-alcoholic fatty liver disease (NAFLD) and low 25(OH) vitamin D levels in an adult population with normal serum liver enzymes. BMC Med. 2011; 9: 85.
20. Targher G, Bertolini L, Scala L, Cigolini M, Zenari L, Falezza G, et al. Associations between serum 25-hydroxyvitamin D3 concentrations and liver histology in patients with non-alcoholic fatty liver disease. Nutr Metab Cardiovasc Dis 2007;17:517-524
21. Ford ES, Ajani UA, McGuire LC, Liu S. Concentrations of serum vitamin D and the metabolic syndrome among US adults. Diabetes Care. 2005; 28:1228-30.
22. Katz K, Brar PC, Parekh N, Liu YH, Weitzman M. Suspected nonalcoholic Fatty liver disease is not associated with vitamin d status in adolescents after adjustment for obesity. J Obes. 2010:496829.
23. Singh SP, Kar SK, Panigrahi MK, Misra B, Pattnaik K, et al. Profile of patients with incidentally detected nonalcoholic fatty liver disease (IDNAFLD) in coastal eastern India. Trop Gastroenterol. 2013; 34: 144-152.
24. J. Ludwig, T. R. Viggiano, D. B. McGill, and B. J. Ott, "Nonalcoholic steatohepatitis. Mayo Clinic experiences with a hitherto unnamed disease," Mayo Clinic Proceedings, 1980; 55(7): 434–438, 1980
25. Gore RM. Diffuse liver disease. In: Gore RM, Levine MS, Laufer I, eds. In: Textbook of Gastrointestinal Radiology. Philadelphia: WB Saunders; 1994:1968–2017.
26. Tietz NW, ed. Clinical Guide to Laboratory Tests, 4th ed. Philadelphia. WB Saunders Company, 2006; 444-451.
27. Kwok, R.M.; Torres, D.M.; Harrison, S.A. Vitamin D and nonalcoholic fatty liver disease (NAFLD): Is it more than just an association? Hepatology. 2013; 58: 1166–1174.

28. Roth, C.L.; Elfers, C.T.; Figlewicz, D.P.; Melhorn, S.J.; Morton, G.J.; Hoofnagle, A.; Yeh, M.M.; Nelson, J.E.; Kowdley, K.V. Vitamin D deficiency in obese rats exacerbates nonalcoholic fatty liver disease and increases hepatic resistin and toll-like receptor activation. Hepatology 2012; 55: 1103–1111.
29. Li, J.; Cordero, P.; Nguyen, V.; Oben, J.A. The role of vitamins in the pathogenesis of non-alcoholic fatty liver disease. Integr. Med. Insights 2016; 11: 19–25.
30. Bril, F.; Maximos, M.; Portillo-Sanchez, P.; Biernacki, D.; Lomonaco, R.; Subbarayan, S.; Correa, M.; Lo, M.; Suman, A.; Cusi, K. Relationship of vitamin D with insulin resistance and disease severity in non-alcoholic steatohepatitis. J. Hepatol. 2015; 62: 405–411.
31. 30.Hao, Y.P.; Ma, X.J.; Luo, Y.Q.; Ni, J.; Dou, J.X.; Hu, Y.Q.; Zhu, J.A.; Bao, Y.Q.; Jia, W.P. Serum vitamin D is associated with non-alcoholic fatty liver disease in chinese males with normal weight and liver enzymes. Acta Pharmacol. Sinica 2014; 35: 1150–1156.
32. Chung GE, Kim D, Kwak MS, Yang JI, Yim JY, et al. (2016) The serum vitamin D level is inversely correlated with nonalcoholic fatty liver disease. Clin Mol Hepatol 22: 146-151.
33. 32 .Li, L.; Zhang, L.; Pan, S.; Wu, X.; Yin, X. No significant association between vitamin D and nonalcoholic fatty liver disease in a chinese population. Dig. Dis. Sci. 2013; 58: 2376–2382.
34. Seo JA, Eun CR, Cho H, et al. Low vitamin D status is associated with nonalcoholic fatty liver disease independent of visceral obesity in Korean adults. PLoS One 2013;8:e75197
35. Ashutosh S. Naniwadekar. "Nutritional Recommendations for Patients with Non- Alcoholic Fatty Liver Disease: An Evidence Based Review". Nutrition issues ingastroenterology, series
36. Scherer, P.E. Adipose tissue: From lipid storage compartment to endocrine organ. Diabetes 2006; 55: 1537–1545.
37. Bedogni, G.; Miglioli, L.; Masutti, F.; Tiribelli, C.; Marchesini, G.; Bellentani, S. Prevalence of and risk factors for nonalcoholic fatty liver disease: The dionysos nutrition and liver study. Hepatology 2005; 42: 44–52.
38. Strauss, R.S.; Barlow, S.E.; Dietz, W.H. Prevalence of abnormal serum aminotransferase values in overweight and obese adolescents. J. Pediatr. 2000; 136: 727–733.
39. Targher G, Bertolini L, Scala L, Cigolini M, Zenari L, Falezza G, et al. Associations between serum 25-hydroxyvitamin D3 concentrations and liver histology in patients with non-alcoholic fatty liver disease. Nutr Metab Cardiovasc Dis 2007; 17:517-524.
40. Mendler M, Turlin B, Moirand R, Jouanolle A, Sapey T, Guyader D, Le Gall J, Brissot P, David V,Deugnier Y. Insulin resistance-associated hepatic iron overload. Gastroenterology 1999; 117:1155-63.
41. George D, Goldwurm S, MacDonald G, Cowley L, Walker N, Ward P, Jazwinska E, Powell L. Increased hepatic iron concentration in non-alcoholic steatohepatitis is associated with increased fibrosis. Gastroenterology 1998; 114: 311-8.
42. Mirshahi F, Cheung O, Natarajan R, Maher J, Kellum J, Sanyal A. Activation and dysregulation of the unfolded protein response in nonalcoholic fatty liver disease. Gastroenterology 2008; 134:568-76.