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RESEARCH ARTICLE
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EFFECT OF VITAMIN D ON LIVER ENZYMES AND NAFLD

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Abstract

Background: NAFLD is one of the metabolic diseases of liver that can lead to variety of complications ranging from simple derangement in liver function to full blown cirrhosis.

Objective: To assess the effect of Vitamin D on liver function and NAFLD.

Materials & Methods: This cross-sectional study was conducted at MMC General Hospital Peshawar. Proper ethical approval was taken from the research committee of the hospital. The inclusion criteria were patient shaving fatty liver seen on imaging and graded according to criteria by a radiologist. The patients with other causes of liver derangement were excluded sampling. The sample size with non-probability convenient sampling as the technique. The patients were assessed properly and those who met the criteria were given Vitamin D for 8 weeks to assess its effect on liver function tests and grading of fatty liver Descriptive statistics were applied for checking the mean and standard deviation Paired sample test was applied to assess the effect before and after giving Vitamin D with a p value of less than 0.05 as significant.

Results: The mean age of the patients was 38 years with equal male to female ratio. The mean grade of fatty liver was 1.65 with 48.3% having mild steatosis, 38.3 moderate steatosis and 13.3 having severe steatosis while after treatment 38.3 had no steatosis, 46.7 mild steatosis and 15% had moderate steatosis. In terms of liver functions significant improvement were seen in ALT, ALP and bilirubin as reflected by p value of less than 0.05.

Conclusion: Our study concludes that role of vitamin D is instrumental in improving both the grade of fatty liver and liver function as well.

Keywords: NALFD, bilirubin , Vitamin D

INTRODUCTION:

NAFLD has been the cornerstone of the all the diseases leading to end stage liver disease. It can range from simple steatosis to frank cirrhosis and thereby one of the essential indications for liver transplantation when the patient is decompensated.[1] The most used investigation that is readily available and noninvasive as well is routine scan of abdomen that should be done by experienced

radiologists as that is significant base for further investigations and treatment. Burn out NASH is another dilemma that has caught hepatologists off guard and is equally concerning for the patients.[2] People who are type 2 diabetics are already dealing troublesome impaired glycemic control and have to deal with complications such as ischemic heart disease, diabetic retinopathy, chronic kidney disease and dyslipidemias. [3]These patients are more challenging to treat as they are not compliant most of the times with dietary measures and exercise along with drugs such as metformin which makes the situation harder.

The diagnosis of NAFLD requires sound clinical judgment as other causes such as autoimmune hepatitis and ALT/AST ratio which is more than 2 in cases of alcoholic liver disease need to be ruled out diligently .The need for liver biopsy can be avoided by using noninvasive scan such as fibro scan that is available in specialized centers. [4] The management of NALFD has to be multidisciplinary with close collaboration between hepatologist, endocrinologist and dietician. There are several recognized treatments for NAFLD and one of the them that needs further research is vitamin D as it easily used by the patients with minimal side effects .[5] So the objective of this study is to assess the effect of Vitamin D on liver function and NAFLD.

MATERIALS & METHODS

This cross-sectional study was conducted at MMC General Hospital Peshawar. Proper ethical approval was taken from the research committee of the hospital. The inclusion criteria were patients having fatty liver seen on imaging and graded according to criteria by a radiologist. The patients with other causes of liver derangement were excluded sampling. The sample size was 60 with non-probability convenient sampling as the technique. The patients were assessed properly and those who met the criteria were given Vitamin D for 8 weeks to assess its effect on liver function tests and grading of fatty liver Descriptive statistics were applied for checking the mean and standard deviation .Paired sample test was applied to assess the effect before and after giving Vitamin D with a p value of less than 0.05 as significant.

RESULTS:

The mean age of the patients was 38 years with equal male to female ratio. The mean grade of fatty liver was 1.65 with 48.3% having mild steatosis ,38.3 moderate steatosis and 13.3 having severe steatosis while after treatment 38.3% had no steatosis ,46.7% mild steatosis and 15% had moderate steatosis . The mean ALT before therapy was 83.15 before administration of vitamin D and 58.53 after it. Similarly the mean ALP and bilribun were 275 and 1.27 and after therapy 239 and 0.0 respectively . CI for ALT (17.7-31.44), AST, ALP(26.19-45.20) and bilirubin(0.279 -0.454) respectively In terms of liver functions significant improvement were seen in ALT, ALP and bilirubin as reflected by p value of less than 0.05

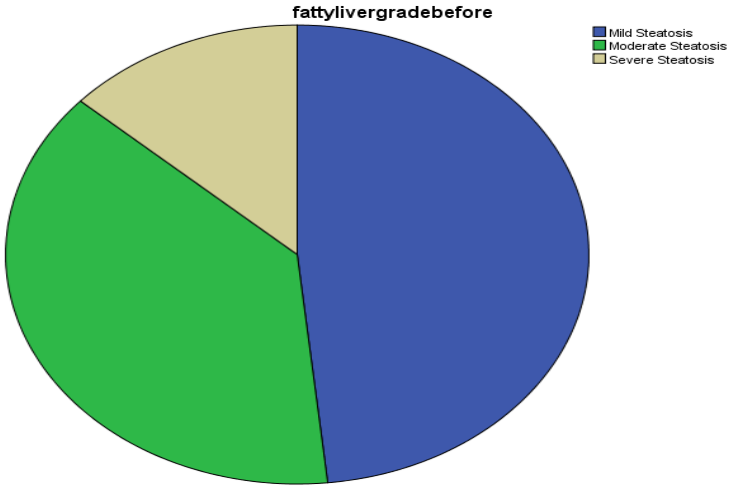
Statistics

Age

N	Valid	60
	Missing	0
Mean		38.45
Minimum		18
Maximum		67

Fatty liver grade before

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Mild Steatosis	29	48.3	48.3	48.3
	Moderate Steatosis	23	38.3	38.3	86.7
	Severe Steatosis	8	13.3	13.3	100.0
	Total	60	100.0	100.0	



Fatty liver grade after

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No Steatosis	23	38.3	38.3	38.3
	Mild Steatosis	28	46.7	46.7	85.0
	Moderate Steatosis	9	15.0	15.0	100.0
	Total	60	100.0	100.0	

Descriptive Statistics

	N	Minimum	Maximum	Mean		Std. Deviation
	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
fatty liver grade before	60	1.00	3.00	1.6500	.09152	.70890
ALT1	60	30.00	200.00	83.1500	5.02911	38.95535
ALP1	60	125.00	495.00	275.4833	8.96542	69.44587
BIL1	60	.50	2.50	1.2700	.06379	.49414
Valid N (listwise)	60					

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
fatty liver grade after	60	.00	2.00	.7667	.69786
ALT2	60	20.00	130.00	58.5333	24.36061
ALP2	60	121.00	340.00	239.7833	59.21953
BIL2	60	.50	1.70	.9033	.29913
Valid N (listwise)	60				

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	fatty liver grade before	1.6500	60	.70890	.09152
	fatty liver grade after	.7667	60	.69786	.09009
Pair 2	ALT1	83.1500	60	38.95535	5.02911
	ALT2	58.5333	60	24.36061	3.14494
Pair 3	ALP1	275.4833	60	69.44587	8.96542
	ALP2	239.7833	60	59.21953	7.64521
Pair 4	BIL1	1.2700	60	.49414	.06379
	BIL2	.9033	60	.29913	.03862

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Fatty liver grade before – fatty liver grade after	.88333	.52373	.06761	.74804	1.01863	13.064	59	.000
Pair 2	ALT1 - ALT2	24.61667	26.44219	3.41367	17.78592	31.44741	7.211	59	.000
Pair 3	ALP1 - ALP2	35.70000	36.78398	4.74879	26.19769	45.20231	7.518	59	.000
Pair 4	BIL1 - BIL2	.36667	.33882	.04374	.27914	.45419	8.382	59	.000

DISCUSSION:

According to most of the systematic reviews patients of NALFD had comparatively decreased levels of vitamin D in contrast to controls. [6]Scientists believe that decreased of vitamin D does lead to progression in the stage of fatty liver and eventual development of chronic liver disease.[7]

A study done in rats came to a conclusion that dietary deficiency can develop and worsen NALFD. [8]And some authors that this is due to inflammation of liver cells resulting in the disease. Another animal study revealed that providing Vitamin D can slow down process of fat deposition in rat models by reducing the inflammation of liver cells as well as fibrosis. It can further via its influence on peroxisome proliferator-activated receptor, will alter the metabolism of free fatty acids , and subsequent reduction in insulin resistance .Further it can inhibit the action of inflammatory mediators thereby decreasing the development of NALFD. [8]A study conducted by Barchetta *et al*., who used 2000 IU/day cholecalciferol didn't affect mediators of inflammation Patients of this study were type 2 diabetics with NAFLD indicating the need for further studies on this matter.[9]

New evidence about Vitamin D says that it can hamper activation stellate cells of liver which is responsible for increasing transformation and proliferation of cells .[5]Another study has proven Vitamin D to have antifibrotic characteristics. The emergence of vitamin D receptor in inflammatory cells in the liver biopsies was seen in patients of NASH and the result did prove mutation of VDR gene, which proved that Vitamin D synthesis and activation is linked with development of NAFLD . According to a study by Lorvand Amiri *et al*., utilizing Vitamin D as calcitriol was more useful when compared with other researches that used it as cholecalciferol. In a total of five researches which assessed the effect of Vitamin D on liver enzymes, only that of Lorvand Amiri *et al*., reported that that supplementation of it can decrease liver enzymes .Using active form of Vitamin D has useful of it on liver enzymes.[10]

Obesity is a known for causing NASH. There is a strong relationship between increase in BMI and advancement of NASH. [11]Therefore, measuring the variables like blood sugar level, weight and lipid profile can play an important role in determining the severity of the disease. As per the results of a recent meta-analysis, deficiency of Vitamin D is linked with enhancement of BMI.[12]The results of the current study showed that the mean grade of fatty liver was 1.65 with 48.3% having mild steatosis ,38.3 moderate steatosis and 13.3 having severe steatosis while after treatment 38.3% had no steatosis ,46.7% mild steatosis and 15% had moderate steatosis . The mean ALT before therapy was 83.15 before administration of vitamin D and 58.53 after it. The results of another meta-analysis proved that Vitamin D without any calorie restriction cant decrease adiposity measures.[13]

All the studies which did evaluate its effect on fats reported significant effect of Vitamin D on levels of lipid except Barchetta *et al*. study, which negated it **Stengths & Limitations:** This study was cross sectional with a relatively small sample size. There is a need for doing multi center trails which will further give credence to this effect of vitamin D on NAFLD and convince primary care physicians to prescribe it regularly to patients.[12]

Conclusion

Our study concludes that role of vitamin D is instrumental in improving both the grade of fatty liver and liver function as well.

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