

Effect of Probiotics on Liver Enzymes and Non Alcoholic Fatty Liver Disease

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ABSTRACT

Objective: To determine the effect of probiotics on liver enzymes and NAFLD.

Study Design: cross sectional study

Place and Duration of Study: This study was conducted at the General Hospital Peshawar from 05th January 2022 to 05th January 2023.

Materials and Methods: The inclusion criteria were patients of NALFD diagnosed on Ultrasound abdomen and on the basis of clinical history. The patients having deranged liver function tests due to other causes such as chronic liver disease, autoimmune hepatitis, drug induced liver injury were excluded from the study. The sample size was 50 and non probability convenient sampling. All the patients had a baseline US abdomen with proper grading of fatty liver documented and liver functions being done. The US Abdomen and liver functions tests were repeated after three months of probiotics as an intervention. The data analysis was done by SPSS version 22. The frequencies and percentages were applied for categorical data where as Mean and SD were applied for quantitative data. Paired sample test was used for comparison of one group before and after intervention with emphasis on mean difference, confidence interval and p value of 0.05 or less as significance.

Results: The mean age of the patients was 40 years with a range from 17 to 67. The mean grade of fatty liver before giving probiotics was 2 with ALT 80.86 ALP 280.42 and bilirubin 1.2. The standard error of mean for ALT, ALP and bilirubin were 5.02, 10.27 and .058 respectively. After giving probiotics the mean ALT was 59.94 ALP 239.24 and bilirubin 0.9. The standard error of mean for ALT, ALP and bilirubin was 3.2, 7.99 and .036 respectively. The mean difference for fatty liver grade 1.3, ALT 24.92, ALP 42.18 and Bilirubin 0.26. The Confidence interval for fatty liver grade ranged from 1.04163 to 1.55837, ALT (17.91 to 30.92), ALP 932.01 to 50.32 and bilirubin 0.174 to 0.345. The p value for grade of fatty liver, ALT, ALP and bilirubin before and after intervention was highly significant as reflected its reading of very low value than 0.05.

Conclusion: In the light of these results probiotics have a beneficial effect in terms of improving fatty liver grade and liver function.

Key Words: NAFLD, probiotics, liver enzymes

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INTRODUCTION

NAFLD is a liver disease known globally and is an integral segment of metabolic syndrome along with obesity and type 2 diabetes mellitus.¹ Fatty liver is one of the most common and well encountered findings on scan done by radiologists as part of routine investigations advised by physician in the light of

deranged liver function tests.² While there are several causes of derangement in liver functions such as acute hepatitis, chronic liver disease, liver cirrhosis, hepatocellular cancer, obstructive jaundice and many others, nonalcoholic fatty liver disease has been deprived of appropriate attention by the gastroenterologists. There has been rapid advancement in hepatology and fatty liver disease management has been the lynchpin for the researchers to discover.

NAFLD though seems a benign disease has really astonished the world in terms of progression to end stage liver disease and even frank cirrhosis resulting in one of the most common reasons for liver transplantation. The prevalence of NALFD has been reported to be 80% according to one study.³ The exact pathogenesis of this disease isn't known but it said that excessive lipid accumulation and insulin resistance are the main culprits. In addition, there is a role of oxidative stress followed per oxidation of lipids resulting in release of inflammatory mediators like

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tumor necrosis factor and cytokines responsible for the disease. Small bowel bacterial growth has also been attributed to have led to non-alcoholic fatty liver disease.⁴

Most of the patients of NALFD are asymptomatic in the beginning apart from being obese. That isn't adequate explanation as it has been seen in thin lean population as well. There is no symptoms such as hematemesis, malena, altered state of consciousness like we see in patients with advanced cirrhosis⁵. So screening of such patients with serial Ultrasounds and liver functions is mandatory after doing a full liver screen including testing for auto antibodies.

There are several treatment modalities for NALFD including metformin and counseling for weight loss. There has been emerging evidence about the role of probiotics which needs research.⁶ So the aim of the study is to assess the effect of probiotics on liver function and NAFLD.

MATERIALS AND METHODS

This cross sectional study was conducted in Peshawar after the approval of research proposal by research committee of MMC General Hospital Peshawar from 05 jan 2022 to 05 jan 2023. The inclusion criteria were patients of NALFD diagnosed on Ultrasound abdomen and on the basis of clinical history . The patients having deranged liver function tests due to other causes such as chronic liver disease ,autoimmune hepatitis, drug induced liver injury were excluded from the study. The sample size was 50 and non probability convenient sampling . All the patients had a baseline US abdomen with proper grading of fatty liver documented and liver functions being done. The US Abdomen and liver

functions tests were repeated after three months of probiotics as an intervention The data analysis was done by SPSS version 22. The frequencies and percentages were applied for categorical data where as Mean and SD was applied for quantitative data. Paired sample test was used for comparison one group before and after intervention with emphasis on mean difference ,confidence interval and p value of 0.05 or less as significance.

RESULTS

The mean age of the patients was 40 years with a range from 17 to 67 .There was equal male to female ratio .The mean grade of fatty liver before giving probiotics was 2 with ALT 80.86 ALP 280.42 and bilirubin 1.2. The standard error of mean for ALT,ALP and bilirubin was 5.02,10.27 and .058 respectively .

After giving probiotics the mean ALT was 59.94 ALP 239.24 and bilirubin 0.9. The standard error of mean for ALT, ALP and bilirubin was 3.2,7.99 and .036 respectively. The mean difference for fatty liver grade 1.3.ALT 24.92,ALP 42.18 and Bilirubin 0.26. The Confidence interval for fatty liver grade ranged from 1.04163 to 1.55837, ALT (17.91 to 30.92),ALP 932.01 to 50.32) and Bilirubin 0.174 to 0.345. The p value for grade of fatty liver. ALT, ALP and bilirubin before and after intervention was highly significant as reflected its reading of very low than 0.05.

Table No. 1: Descriptive Statistics

	N	Minimum	Maximum	Mean
Age	50	17	67	40.52
Valid N (listwise)	50			

Table No. 2: Statistics

		Fatty liver grade before	ALT1	ALP1	BIL1
N	Valid	50	50	50	50
	Missing	0	0	0	0
Mean		2.0000	81.8600	280.4200	1.2060
Std. Error of Mean		.08571	5.02744	10.27313	.05830
Median		2.0000	73.5000	286.0000	1.2000
Mode		2.00	48.00 ^a	278.00 ^a	1.20
Std. Deviation		.60609	35.54934	72.64200	.41227
Minimum		1.00	25.00	119.00	.50
Maximum		3.00	200.00	495.00	2.30

a. Multiple modes exist. The smallest value is shown

Table No.3: Statistics

		Fatty Liver Grade After	ALT2	ALP2	BIL2	Age
N	Valid	50	50	50	50	50
	Missing	0	0	0	0	0
Mean		.7000	56.9400	239.2400	.9460	
Std. Error of Mean		.09147	3.28688	7.99273	.03683	
Median		1.0000	52.5000	237.5000	1.0000	
Mode		1.00	55.00	210.00	1.00	
Std. Deviation		.64681	23.24177	56.51713	.26046	

Minimum	.00	20.00	134.00	.50	
Maximum	2.00	115.00	386.00	1.80	

Table No. 4: Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Fatty liver grade before	2.0000	50	.60609	.08571
	Fatty liver grade after	.7000	50	.64681	.09147
Pair 2	ALT1	81.8600	50	35.54934	5.02744
	ALT2	56.9400	50	23.24177	3.28688
Pair 3	ALP1	280.4200	50	72.64200	10.27313
	ALP2	239.2400	50	56.51713	7.99273
Pair 4	BIL1	1.2060	50	.41227	.05830
	BIL2	.9460	50	.26046	.03683

Table No. 5: Paired samples Correlations

		N	Correlation	Sig.
Pair 1	Fatty liver grade before & fatty liver grade after	50	-.052	.720
Pair 2	ALT1 & ALT2	50	.724	.000
Pair 3	ALP1 & ALP2	50	.905	.000
Pair 4	BIL1 & BIL2	50	.682	.000

Table No. 6: 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	1.30000	.90914	.12857	1.04163	1.55837	10.111	49	.000
Pair 2	ALT1 - ALT2	24.92000	24.63931	3.48452	17.91759	31.92241	7.152	49	.000
Pair 3	ALP1 - ALP2	41.18000	32.24124	4.55960	32.01714	50.34286	9.031	49	.000
Pair 4	BIL1 - BIL2	.26000	.30237	.04276	.17407	.34593	6.080	49	.000

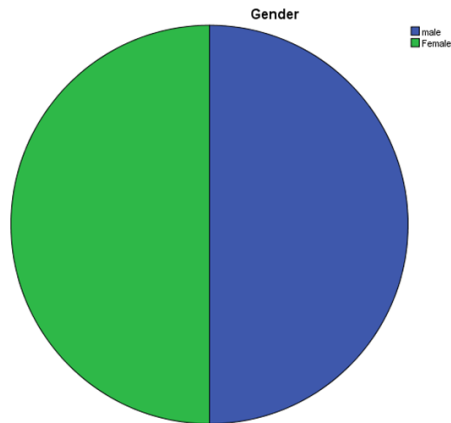


Figure No. 1: Gender

DISCUSSION

NAFLD is defined as greater accumulation of triglycerides in the absence of heavy drinking, other etiologies such as Wilson disease, infectious hepatitis, primary biliary cirrhosis.⁷ It is characterized by ballooning degeneration of hepatocytes and eventual fibrosis. NAFLD is a matter of concern as it is a silent disease and burnt out NASH can lead to cirrhosis in a

short period of time.⁸ Around 80 to 100 million adult population are victims of NAFLD in the United States. About 20% of NAFLD do suffer from nonalcoholic steatohepatitis (NASH) in western countries. In addition, the prevalence of NAFLD is about 15% in Chinese adults with 1.3% reported in children.⁹ Previous researches did report that consuming probiotic yogurt does improve lipid profile, glycemic control, hepatic enzymes, and steatosis on ultrasound. In addition, earlier studies did employ ultrasound being non invasive and cheaper than other investigations to estimate liver fat.¹⁰ According to research high potency multistrain probiotics leads to improvement in histology of liver in non-alcoholic fatty liver disease (NAFLD): 30 (76.9%) in a total 39 subjects with NAFLD did complete the study with extensive 12 months follow-up. A liver biopsy got repeated after this in 10 patients (52.6%) in probiotic group and 5 (25%) in placebo group. When compared to the baseline, the ballooning of hepatocytes (p=0.036), inflammation of lobules (p=0.003) and NAS score (p=0.007) improved by a significant level in the probiotic group. As compared to placebo, the NAS score did get better remarkably in probiotic group (p=0.004), significantly along with incredible

improvements in hepatocyte ballooning ($p=0.05$) and liver fibrosis ($p=0.018$). A remarkable improvement in ALT level ($p=0.46$), leptin ($p=0.006$), TNF- α ($p=0.016$) and endotoxins ($p=0.017$) was also seen in probiotic group.¹¹

Pharmacological treatment for the patients of NAFLD and NASH is continuously evolving. Many guidelines recommend vitamin E or pioglitazone in patients who are not diabetic and have NASH on biopsy however, both of them have long-term sideeffects.¹² Many of new drugs namely obeticholic acid, elafibranor, selonsertib and cenicriviroc have revealed great results in phase II studies results of phase III studies are still awaited.¹³

According to the results of this study after giving probiotics the mean ALT was 59.94 ALP 239.24 and bilirubin 0.9. The standard error of mean for ALT,ALP and bilirubin was 3.2,7.99 and .036 respectively. The mean difference for fatty liver grade 1.3.ALT 24.92,ALP 42.18 and Bilirubin 0.26. The Confidence interval for fatty liver grade ranged from 1.04163 to 1.55837, ALT (17.91 to 30.92),ALP 932.01 to 50.32) and bilirubin 0.174 to 0.345. The p value for grade of fatty liver.ALT,ALP and bilirubin before and after intervention was highly significant as reflected its reading of very low than 0.05.

These results do prove a point the probiotics have a beneficial effect on NAFLD Further studies in this regard can further substantiate our results as probiotics are not harmful and can be used with ease by the patients.

CONCLUSION

In the light of these results probiotics have a positive effect in terms of improving fatty liver grade and liver function.

Author's Contribution:

Concept & Design of Study: Jibran Umar Ayub Khan
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Final Approval of version: Jibran Umar Ayub Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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