

Frequency of Dyslipidemia in Patients Presenting with Nonalcoholic Fatty Liver Disease

MUHAMMAD IMRAN ULLAH¹, GUL-E LALA², RASHID KARIM³, NAYYAR ZAMAN⁴, IBADULLAH JAN⁵, ANNUM SHAHZADI⁶

¹Assistant Professor, Department of Gastroenterology Hayatabad Medical Complex Peshawar

²Specialist Registrar, Department of Pediatric, Hayatabad Medical Complex, Peshawar

³Assistant Professor of Gastroenterology, Department of gastroenterology, DHQ Teaching Hospital and Ghazi Khan Medical College DG Khan, Punjab

⁴Associate professor, Biochemistry Gajju khan Medical college Swabi

⁵Assistant Professor of Pharmacology, College of Veterinary Sciences, The University of Agriculture Peshawar, 25130, Pakistan

⁶Assistant Physician, Department of Dermatology, Federal Government Polyclinic Hospital Islamabad

Corresponding author: Gul-E Lala, Email: gulelala49@gmail.com

ABSTRACT

Introduction: Nonalcoholic fatty liver disease (NAFLD) is one of the most common causes of chronic liver disease in the developed world with increasing incidence among adults and children, and it is estimated to turn out leading cause for liver transplantation in America by end of this year¹ It can present with variety of liver disease from nonalcoholic fatty liver (NAFL) to nonalcoholic steatohepatitis (NASH) and cirrhosis. Purpose of our study is to determine frequency of dyslipidemia in patients with nonalcoholic fatty liver disease², although many studies had already been conducted on the same topic but no such study has been performed in our setup for the last many years. This study will give us the latest magnitude of dyslipidemia in patients with nonalcoholic fatty liver disease in our setup which will result in timely diagnosis, better management and future recommendations.

Objective: To evaluate the frequency of dyslipidemia in patients presenting with nonalcoholic fatty liver disease at Hayatabad Medical Complex, Peshawar.

Material and Methods: This cross sectional descriptive study was carried out at Gastroenterology Department, Hayatabad Medical Complex, Peshawar from 1st January 2022 to 31 June 2022. In the current study a total of 124 patients were observed. All the routine investigation, clinical examination and history were taken from the included patients as per hospital protocol. All the patients were subjected to radiology department for ultrasound of abdomen aimed at confirmation of nonalcoholic fatty liver disease. All radiological examination was done by an expert radiologist (FCPS) having at least 2 years of experience. 5 cc of blood sample was taken from the included patients and was referred to hospital laboratory for the diagnosis of dyslipidemia. Laboratory investigations were entirely done by expert pathologist (FCPS) having at least two years of experience. Dyslipidemia was considered positive if the lipid levels is other than the normal range in one or more laboratory tests.

Results: In this study 22(18%) patients were in age range 18-30 years and 102(82%) patients were in age range 31-60 years. 38(31%) patients were male while 86(69%) patients were female. 33(27%) patients had duration of disease \leq 5 year and 91(73%) patients had duration of disease $>$ 5 year. 38(31%) patients had BMI \leq 25 Kg/m² while 86(69%) patients had BMI $>$ 25 Kg/m². 82(66%) patients were diabetic while 42(34%) patients were not diabetic. 89(72%) patients were hypertensive while 35(28%) patients were not hypertensive. 32(26%) patients had dyslipidemia while 92(74%) patients didn't had dyslipidemia.

Conclusion: Our study concludes that frequency of dyslipidemia was 26% in patients presenting with nonalcoholic fatty liver disease at Hayatabad Medical Complex, Peshawar.

Keywords: dyslipidemia, nonalcoholic, fatty liver disease.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is one of the most common causes of chronic liver disease in the developed world with increasing incidence among grown persons and kids, and it is estimated to become the most common cause for liver transplantation in America by end of this year.¹ It can present with range of liver disease from nonalcoholic fatty liver (NAFL) to nonalcoholic steatohepatitis (NASH) and cirrhosis². NAFL is usually considered as benevolent from the liver standpoint with smallest amount of risk of cirrhosis whereas NASH can evolve to cirrhosis, liver failure, and liver cancer. Major risk factors for NAFLD are obesity, type2 diabetes, and dyslipidemia. Metabolic syndrome is commonly established in patients with NAFLD; it is believed that NAFLD should be reflected as the part of the range of metabolic syndrome.² Dyslipidemia in patients with NAFLD is categorized by augmented levels of serum triglycerides, amplified small, dense low-density lipoprotein (LDL no type A) particles, and low high-density lipoprotein (HDL) cholesterol and considers as highly atherogenic in nature³⁻⁴.

The pathological process of dyslipidemia in NAFLD is not well known, nevertheless it is proposed that very low-density lipoprotein particles are over produced by hepatocyte and process of getting rid of lipoproteins from the circulation is dysregulated⁵. The substantiation that cardiovascular disease is the communal cause of death in patients with NAFLD is unequivocal⁶⁻⁷. The overall supervision of patients with NAFLD is dependant on aggressive treatment of dyslipidemia. The first-line agent remain is statin to treat high cholesterol and their amount should be adjusted based on acceptability and achieving beneficial level. Entirely

statins found to be beneficial in alleviating dyslipidemia levels in patients with NAFLD, but there is more understanding with atorvastatin in patients with NAFLD; furthermore, decrease death related to cardiovascular diseases in patients with NAFLD is only proven with statin⁸. The risk of liver related adverse events from statins is infrequent and patients with NAFLD are not at augmented risk for statin related liver injury.⁹⁻¹⁰ the first choice to treat hypertriglyceridemia is Omega-3 fatty acids due to safety, acceptability, and effectiveness in improving serum triglycerides, as well as effective in improving liver disease. In a study performed by Waqas M et al described that the occurrence of dyslipidemias remained 29%¹¹⁻¹³ in patients with nonalcoholic fatty liver disease.

Aim of our study is to determine frequency of dyslipidemia in patients with nonalcoholic fatty liver disease. Although many studies had already been conducted on the same topic but no such study has been performed in our setup for the last many years. This study will give us the latest magnitude of dyslipidemia in patients with nonalcoholic fatty liver disease in our setup which will result in timely diagnosis, better management and future recommendations.

Objective: To assess the frequency of dyslipidemia in patients presenting with nonalcoholic fatty liver disease at Hayatabad Medical Complex, Peshawar.

MATERIAL AND METHODS

The current study was conducted at Gastroenterology Department, Hayatabad Medical Complex, and Peshawar from 31 January 2022 to 31 June 202. . It was descriptive cross

sectional study. A total 124 patients were included in study after assessing for inclusion and exclusion standards.

Inclusion criteria: All the patients presenting with nonalcoholic fatty liver disease with duration more than six month, patients in age between 18-60 years and both gender were involved in the study.

Exclusion criteria: Entirely patients presentation with history of ischemic heart diseases (assessed on the bases of ECG and ECHO), patients with HBV and HCV (assessed on the basis of HbsAg positive elisa and anti-HCV antibody), patients with history of alcohol consumption (assessed on the bases of history) and patients previously on Lipid lowering drugs or under corticosteroid therapy (assessed on the bases of history) were excluded from the study because they were potential confounders and could lead to bias in study results.

Data Collection Procedure: The current study was carried out after taking permission from hospital ethical committee. All the patients fulfilling the inclusion criteria i.e. Patients presented with nonalcoholic fatty liver disease with duration more than six month patients was enrolled in the study through OPD and Gastroenterology Department of Hayatabad Medical Complex, Peshawar. The purpose and the benefits of the study were clarified and written inform permission was attained from all the included patients at the time of admission.

All the routine investigation, clinical examination and history were taken from the included patients as per hospital protocol. All the patients were subjected to radiology department for ultrasound of abdomen for the confirmation of nonalcoholic fatty liver disease. All the radiological examination was done by an expert radiologist (FCPS) having at least 2 years of experience. 5 cc of blood sample was taken from the included patients and was referred to hospital research laboratory for the diagnosis of dyslipidemia. Altogether the laboratory investigations were done by expert pathologist (FCPS) having at least two years of experience. Dyslipidemia was considered positive if the lipid levels is other than the normal range (given in operational definition) in one or more laboratory tests.

All the data i.e. age, gender, duration of disease, total cholesterol level, low-density lipoprotein level, triglycerides level, high-density lipoprotein level, weight, height, BMI, hypertension, diabetes mellitus was recorded in Performa. Exclusion criteria had strictly followed to avoid bias in study results.

Data Analysis: All the recorded data in Performa was entered in statistical software SPSS and descriptive analysis was performed. Mean and standard deviation was calculated for quantitative variables i.e. age, duration of disease, total cholesterol level, low-density lipoprotein level, triglycerides level, high-density lipoprotein level, height, weight, BMI. Frequencies and percentages were computed for qualitative variables like gender, diabetes mellitus, hypertension and dyslipidemia. Dyslipidemia was stratified with effect modifiers like age, gender, duration of disease, BMI, hypertension and diabetes mellitus to see outcome modifications. Chi square test was applied for post stratification in which P value ≤ 0.05 was reflected as significant value.

RESULTS

In this study 22(18%) patients were in age range 18-30 years and 102(82%) patients were in age range 31-60 years. (Table no 1) 38(31%) patients were male while 86(69%) patients were female. (Table no 2). 33(27%) patients had duration of disease ≤ 5 year and 91(73%) patients had duration of disease > 5 year. (Table no 3). 38(31%) patients had BMI ≤ 25 Kg/m² while 86(69%) patients had BMI > 25 Kg/m². (Table no 4). 82(66%) patients were diabetic while 42(34%) patients were not diabetic. (Table no 5). 89(72%) patients were hypertensive while 35(28%) patients were not hypertensive. (Table no 6). 32(26%) patients had dyslipidemia while 92(74%) patients didn't had dyslipidemia. (Table no 7). Stratification of dyslipidemia with respect to age, gender, duration of disease, BMI, hypertension and diabetes mellitus is given in table no (8-13)

Table 1: Age Distribution

Age	Frequency	Percentage
18-30 Years	22	18%
31-60 Years	102	82%
Total	124	100%

Mean age was 55 years with SD ± 9.39

Table 2: Gender Distribution

Gender	Frequency	Percentage
Male	38	31%
Female	86	69%
Total	124	100%

Table 3: Duration of Disease

Duration	Frequency	Percentage
≤ 5 Years	33	27%
> 5 Years	91	73%
Total	124	100%

Table 4: BMI Distribution

BMI	Frequency	Percentage
≤ 25 kg/m ²	38	31%
> 25 kg/m ²	86	69%
Total	124	100%

Mean BMI was 25 kg/m² with SD $\pm \leq 5.93$

Mean height was 1.6 meters with SD ± 1.10

Mean weight was 85 Kg with SD ± 13.11

Table 5: Diabetes Niellitus

Diabetes Niellitus	Frequency	Percentage
Diabetic	82	66%
Non-Diabetic	42	34%
Total	124	100%

Table 6: Hypertension

Hypertension	Frequency	Percentage
Hypertensive	89	72%
Non Hypertensive	35	28%
Total	124	100%

Table 7:

Dyslipidemia	Frequency	Percentage
Yes	32	26%
Non Hypertensive	92	74%
Total	124	100%

Mean Total cholesterol was 187 mg/dL ± 20.31

Mean Low-density lipoprotein was 123 mg/dL ± 24.68

Mean Triglycerides was 125 mg/dL ± 18.29

Mean High-density lipoprotein was 58 mg/dL ± 7.45

Table 8: Stratification of Dyslipideivha with Respect to Age Distribution

Dyslipidemia	18-30 years	31-60 years	Total	P value
Yes	6	26	32	0.8624
No	16	76	92	
Total	22	102	124	

Table 9: Stratification of Dyslipidemia with Respect to Gender Distribution

Dyslipidemia	Male	Female	Total	P value
Yes	10	24	32	0.9313
No	28	64	92	
Total	38	86	124	

Table 10: Stratification of Dyslipidemia with Respect to Duration of Disease

Dyslipidemia	< 5 years	> 5 years	Total	P value
Yes	9	23	32	0.8222
No	24	68	92	
Total	33	91	124	

Table 11: Stratification of Dyslipidemia with Respect to BMI Distribution

Dyslipidemia	≤ 25 Kg/m ²	> 25 Kg/m ²	Total	P value
Yes	10	22	32	0.9313
No	28	64	92	
Total	38	86	124	

Table 12: Stratification of Dyslipidemia with Respect to Diabetes Mellitus

Dyslipidemia	Diabetic	Non	Total	P value
Yes	21	11		0.9442
No	61	31	92	
Total	82	42	124	

Table 13: Stratification of Dyslipidemia with Respect to Hypertension

Dyslipidemia	Hypertensive	Non Hypertensive	Total	P value
Yes	23	9	32	0.9882
No	66	26	92	
Total	89	35	124	

DISCUSSION

Nonalcoholic fatty liver disease (NAFLD) is one of the leading origins of chronic liver disease in the developed world with increasing incidence among adults and children, and it is predicted to become the leading cause for liver transplantation in America by end of this year.¹

It can present with range of liver disease from nonalcoholic fatty liver (NAFL) to nonalcoholic steatohepatitis (NASH) and cirrhosis². NAFL is usually considered as benevolent from the liver standpoint with smallest amount of risk of cirrhosis whereas NASH can evolve to cirrhosis, liver failure, and liver cancer. Major risk factors for NAFLD are obesity, type2 diabetes, and dyslipidemia. Metabolic syndrome is commonly established in patients with NAFLD; it is believed that NAFLD should be reflected as the part of the range of metabolic syndrome.² Dyslipidemia in patients with NAFLD is categorized by augmented levels of serum triglycerides, amplified small, dense low-density lipoprotein (LDL non-type A) particles, and low high-density lipoprotein (HDL) cholesterol and considers as highly atherogenic in nature³⁻⁴.

In this study 22(18%) patients were in age range 18-30 years and 102(82%) patients were in age range 31-60 years. 38(31%) patients were male while 86(69%) patients were female. 33(27%) patients had duration of disease ≤ 5 year and 91(73%) patients had duration of disease > 5 year. 38(31%) patients had BMI ≤ 25 Kg/m² while 86(69%) patients had BMI >25 Kg/m². 82(66%) patients were diabetic while 42(34%) patients were not diabetic. 89(72%) patients were hypertensive while 35(28%) patients were not hypertensive. 32(26%) patients had dyslipidemia while 92(74%) patients didn't had dyslipidemia.

Comparable results were detected in another study conducted by Waqas M et al¹⁴⁻¹⁵ in which 68(68%) were between 20-50 years of age while 32(32%) were between 51-70 years of age with mean was 44.68±11.57 years, 55(55%) were male and 44(44%) were females. Frequency of dyslipidemia in non-alcoholic fatty liver disease was recorded in 29(29%) while 71(71%) had no findings of the morbidity.

In another study conducted by Unger LW et al¹⁶ had reported that among all reasons, total cholesterol levels were considerably lower in ACLD, when matched to non-ACLD. Consequently, LDL-cholesterol levels were considerably lower in ACLD due to hepatitis C, hepatitis B, metabolic/fatty liver disease and autoimmune hepatitis. Disease severity did not have any impact on level of triglyceride in any etiology. Specific dyslipidemia pattern by etiology stayed equal to non ACLD regardless of of lower total and LDH cholesterol level in ACLD.. Conflicting to this "better" lipid status in ACLD, cardiovascular related diseases were more predominant in ACLD: arterial hypertension was present in 26.6% of non-ACLD and in 55.4% of ACLD patients (p<0.001), and diabetes was present in 8.1% of non-ACLD and 25.6% of ACLD patients (p<0.001).

Higher prevalence of fatty liver in urban higher societies is mainly due to development and urbanization. The percentage of NAFLD in urban and rural parts of Pakistan were 27%, 15, 9 and 42%, 27, 21 among higher middle and lower cultures respectively¹⁷.

In patients with DM type-2 and MS in our society the frequency related to NAFLD was around 72.4%.¹⁸ the relationship

of raised ALT level of unknown reasons with NAFLD was 13.5% in a study conducted by Niaz et al¹⁹ Previous research revealed that 49.5% cases with raised ALT had NAFLD²⁰. The higher prevalence of NAFLD in public especially with female's preponderance was mainly due to presence of obesity, hepatomegaly, diabetes, and hypertriglyceridemia in a research conducted by Khurram and Ashraf²¹. In presentation with fatigability among NAFLD patients, 38% cases had NASH. Old age and high BMI were commonly present in patients with NAFLD compare to control group in a study being conducted by Abbas et al²². In patients with NAFLD 21.8% were found to have elevated aminotransferase and NASH²³. The frequency of NAFLD in a study by Luxmi et al among diabetics was around 60.8%, which was comparable with study conducted by Gupte et al²⁴ in India which showed it 49%. Independant predictor of fatty liver was associated with high BMI .Diabetes was risk factor for NAFLD and occurrence of NAFLD among diabetic was found to be 51% and elevated triglyceride was risk factor for NAFLD (51% prevalence) and heaviness in right upper quadrant (64.7%).was the most common symptom in a study carried out by Taseer et al²⁵.

CONCLUSION

Our study concludes that frequency of dyslipidemia was 26% in patients presenting with nonalcoholic fatty liver disease at Hayatabad Medical Complex, Peshawar.

REFERENCES

- Lazo M, Hernaez R, Eberhardt MS, Bonekamp S, Kamel I, Guallar E, et al. Prevalence of nonalcoholic fatty liver disease in the United States. *Am J Epidemiol* 2015;178:38-45
- Eslam M, Valenti L, Romeo S. Genetics and epigenetics of NAFLD and NASH: clinical impact. *J Hepatol.* 2018;68(2):268-79
- Cusi K, Chang Z, Harrison S, Zali MR. Non-alcohol fatty liver disease as a biomarker for NASH and fibrosis in patients with non-alcoholic fatty liver disease. *J Hepatol.* 2016;60(1):167-74.
- Ashtari S, Pourhoseingholi MA, Zali MR. Non-alcohol fatty liver disease in Asia: prevention and planning. *World J Hepatol.* 2015;7(13):1788.
- Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of non-alcoholic fatty liver disease-meta-analytic assessment of prevalence, incidence and outcomes. *Hepatology.* 2016;64(1):73.
- Angulo P, Kleiner DE, Dam-Larsen S, et al. Liver fibrosis, but no other histologic features, is associated with long-term outcomes of patients with nonalcoholic fatty liver disease. *Gastroenterology.* 2015;149(2):389-397.e10.
- Ghani RA, Saqlain M, Zafar MM, Jabeen S, Naqvi SMS, Raja GK. Identification of metabolic risk phenotypes predisposing to non-alcoholic fatty liver disease in a Pakistani cohort. *Pak J Med Sci.* 2017;33(1):121.
- Corey KE, Chalasani N. Management of dyslipidemia as a cardiovascular risk factor in individuals with nonalcoholic fatty liver disease. *Clin Gastroenterol Hepatol.* 2014;12(7):1077-84.
- Waqas M, Shah NU, Achakzai MS, Tayyab GN. Frequency of dyslipidemia in non alcoholic fatty liver disease patients. *Pak J Med Health Sci.* 2017;11(1):111-13.
- Saadeh S, Younossi ZM, Remer EM, et al. The utility of radiological imaging in nonalcoholic fatty liver disease. *Gastroenterology* 2002;123:745-50.
- Paschos P, Paletas K. Non alcoholic fatty liver disease and metabolic syndrome. *Hippokratia* 2009;13:9-19.
- Palmentieri B, de Sio I, La Mura V. The role of bright liver echo pattern on ultrasound B-mode examination in the diagnosis of liver steatosis. *Dig Liver Dis* 2017;38:485-89.
- Karcaaltincaba M, Akhan O. Imaging of hepatic steatosis and fatty sparing. *Eur J Radiol* 2016;61:33-43.
- Fierbinteanu-Braticevici C, Dina I, Petrisor A, Tribus L, Negreanu L, Carstoiu C. Noninvasive investigations for non alcoholic fatty liver disease and liver fibrosis. *World J Gastroenterol* 2015;16:4784-91.
- Tarantino G, Pizza G, Colao A, Pasanisi F, Conca P, Colicchio P, Finelli C, Contaldo F, Di Somma C, Savastano S. Hepatic steatosis in overweight/obese females: new screening method for those at risk. *World J Gastroenterol* 2016; 15: 5693-5699.
- Iwasaki M, Takada Y, Hayashi M. Noninvasive evaluation of graft steatosis in living donor liver transplantation. *Transplantation* 2015;78:1501-5.

17. Park SH, Kim PN, Kim KW. Macrovesicular hepatic steatosis in living liver donors: use of CT for quantitative and qualitative assessment. *Radiology* 2017;239:105–12.
18. Fierbinteanu C, Dina I, Petrisor A, Tribus L, Negreanu L, Carstoiu C. Noninvasive investigations for non alcoholic fatty liver disease and liver fibrosis. *World J Gastroenterol* 2015;16:4784-91.
19. Wieckowska A, McCullough AJ, Feldstein AE. Noninvasive diagnosis and monitoring of nonalcoholic steatohepatitis: present and future. *Hepatology* 2015; 46: 582-589
20. Oh MK, Winn J, Poordad F. Review article: diagnosis and treatment of non-alcoholic fatty liver disease. *Aliment Pharmacol Ther* 2016;28:503-522.
21. Yoneda M, Mawatari H, Fujita K, Iida H, Yonemitsu K, Kato S, et al. High-sensitivity C-reactive protein is an independent clinical feature of nonalcoholic steatohepatitis (NASH) and also of the severity of fibrosis in NASH. *J Gastroenterol* 2015;42: 573-82.
22. Wieckowska A, Papouchado BG, Li Z, Lopez R, Zein NN, Feldstein AE. Increased hepatic and circulating interleukin-6 levels in human nonalcoholic steatohepatitis. *Am J Gastroenterol* 2016;103:1372-79.
23. Yoneda M, Uchiyama T, Kato S A. Plasma Pentraxin3 is a novel marker for nonalcoholic steatohepatitis (NASH). *BMC Gastroenterol* 2014; 8: 53
24. Satapathy SK, Sakhujia P, Malhotra V, Sharma BC, Sarin SK. Beneficial effects of pentoxifylline on hepatic steatosis, fibrosis and necroinflammation in patients with non-alcoholic steatohepatitis. *J Gastroenterol Hepatol* 2015;22:634-8.
25. Tarantino G, Mazzearella C, Tarantino M, Di Minno MN, Conca P. Could high levels of tissue polypeptide specific antigen, a marker of apoptosis detected in nonalcoholic steatohepatitis, improve after weight loss? *Dis Markers* 2009;26:55-63.