

The Risk Factors Associated with Non-Alcoholic Fatty Liver Disease

HASSAN MAHMOOD¹, MADIHA ABBAS², MARIAM AZEEM³, IRFAN YOUNUS⁴, ADNAN QADIR⁵, MUHAMMAD HABIB⁶

¹Assistant Professor of Medicine, KEMU/ Mayo Hospital Lahore

²Senior Registrar, Mayo Hospital Lahore

³Senior Registrar Medicine, Mayo Hospital Lahore

⁴AP Gastroenterology, Nawaz Sharif Medical College Gujrat

⁵AP Gastroenterology, Islamic International Medical College Rawalpindi

⁶Medical Officer Mayo Hospital Lahore

Corresponding author: Irfan Younus, Email: irfanyounis7887@gmail.com

ABSTRACT

Background: While non-alcoholic fatty liver disease (NAFLD) is a widespread illness that affects many people in Pakistan, little is known about its epidemiology. Although a large number of individuals have NAFLD risk factors, only a tiny proportion go on to develop serious liver conditions including cirrhosis or hepatocellular carcinoma. Identification of people who are most likely to have these consequences is essential since it will allow medical personnel to spot and address risk factors early on and, eventually, stop the illness from progressing.

Objective: The purpose of this research is to look at the risk factors for NAFLD at Mayo Hospital Lahore, Pakistan. We intend to learn more about the occurrence and NAFLD risk factors in this community by performing this research. Our ultimate objective is to enhance NAFLD prevention and treatment in Pakistan, which would enhance the health outcomes for those who are afflicted.

Methods: From July 2022 to December 2022, a meticulous cross-sectional investigation was carried out at the esteemed Mayo Hospital in Lahore, Pakistan, to scrutinize the risk factors responsible for the onset of non-alcoholic fatty liver disease (NAFLD). The study cohort, comprising 35 participants, was selected with great care and prudence to ensure their suitability and relevance to the research question at hand. This study aimed to unravel the intricate web of risk factors associated with NAFLD, which has emerged as a global health concern.

Results: The study conducted at Mayo Hospital in Lahore, Pakistan involved 35 participants who were selected for their relevance to the research question. The study participants had a mean age of 38.89 ± 8.50 years, with the majority being females, accounting for 80% of the sample population. Moreover, a significant proportion of the participants were housewives, representing 68.6% of the sample. The majority of the participants belonged to the middle-class socioeconomic stratum (60%). The study revealed some intriguing findings, as almost half of the participants (48.6%) had diabetes mellitus (DM) and 42.9% were classified as obese. On average, the study participants had a body weight of 72.74 ± 8.74 units and a body height of 61.37 ± 2.67 units. These findings provide insightful information on the risk factors for NAFLD in the Pakistani community.

Conclusions: Currently, non-alcoholic fatty liver disease (NAFLD) has become the most common cause of chronic liver disease in Pakistan. This alarming trend shows how important it is for doctors and governments to give this increasing menace top priority. Controlling and reducing the harmful health effects of NAFLD in Pakistan requires the implementation of specific public health interventions and preventative initiatives.

Keywords: liver, diabetes, non-alcoholic fatty liver disease

INTRODUCTION

NAFLD is a prevalent health issue worldwide, characterized by excessive lipid accumulation in the liver. If left untreated, it can lead to NASH, causing liver cell destruction and inflammation. NAFLD has become the most common cause of chronic liver disease globally, and its incidence is on the rise due to the increasing prevalence of obesity and type 2 diabetes. [1] NAFLD is a complex condition that can cause a range of health problems. While it is typically asymptomatic, it can result in cirrhosis, hepatocellular carcinoma, and liver failure, among other things. Furthermore, it has been linked to other serious conditions such as cardiovascular disease, diabetes, and metabolic syndrome [2,3]. Consequently, it is important to detect and treat NAFLD as soon as possible to avoid these potentially life-threatening complications.

Research into NAFLD is ongoing, and there is still much to learn about the condition's pathogenesis and the best ways to treat it. However, there are some proven methods for preventing and treating NAFLD. Lifestyle changes such as losing weight, exercising regularly, and adopting a healthy diet can all be effective in reducing the risk of NAFLD and its progression to NASH. In some cases, medication and surgical intervention may also be necessary to manage the condition [4]. Around 30% of those with NAFLD have NASH, which, if mistreated, may result in fibrosis, cirrhosis, and perhaps even hepatocellular carcinoma (HCC) [5]. NAFLD is becoming much more common in the Asia-Pacific area, where up to 30% of the population is affected [5]. Both emerging and developed Asian countries are seeing an increase in the prevalence of NAFLD in adults [6].

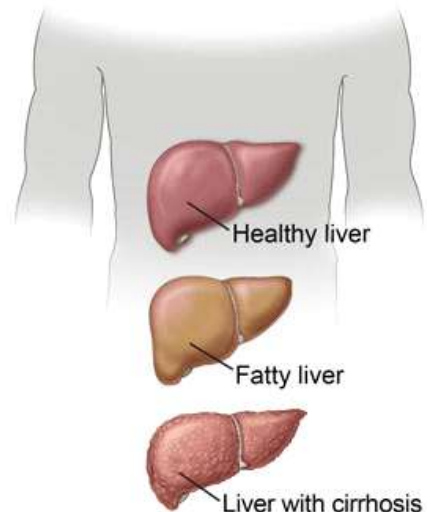


Figure 1: Non-Alcoholic Fatty Liver Disease (NAFLD)

NAFLD is a significant public health concern because of its high incidence, ability to advance to serious liver disease, and relationship to cardio-metabolic conditions such as T2DM,

metabolic disorders, and coronary artery disease (CAD). In Western nations and places with lower BMI, such as Asia, it has emerged as the main contributor to chronic liver disease. The increased incidence of NAFLD has been influenced by the rising rates of metabolic syndrome, diabetes, and obesity in the general population. Hence, early diagnosis and effective management of NAFLD are crucial to reducing the burden of chronic liver disease and its associated complications. A noncommunicable disease pandemic, like NAFLD, has emerged as a result of recent socioeconomic trends including increased prosperity and lifestyle changes. Between 4 to 18.4% of Pakistan's general population are thought to have NAFLD, with diabetics having a prevalence of 49.8% [7]. Rahman et al. discovered a prevalence of 18.4% in their study of a rural population, with a greater frequency of 59.4% among diabetic patients [8].

Medical professionals and health policymakers must pay close attention to Pakistan's high prevalence of NAFLD to research and address this threat as soon as possible. In Mayo Hospital, Lahore, Pakistan, non-alcoholic fatty liver disease risk factors were examined as part of this study's goal.

METHODS

Cross-sectional research was recently carried out at the Mayo Hospital's Department of Hepatology in Lahore, Pakistan. 35 people were included in the study, which ran for six months from September 2022 to February 2023. Each subject voluntarily gave their informed, written consent to take part in the research. The objective of this study was to assess the occurrence of non-alcoholic fatty liver disease (NAFLD) and identify its related risk factors in the local community. Each subject had a thorough physical examination, and the study team methodically recorded the results on an organized datasheet. To confirm the correctness of the data, the researchers also extensively monitored each person's blood pressure readings in various situations. Also, the researchers determined each participant's body mass index (BMI) by taking their weight and height while they were standing on a scale with their feet about 15 cm apart and their weight uniformly distributed on both legs. The researchers used a specialized liver ultrasonography device called FibroScan to assess the extent of fibrosis and steatosis in the individuals. As it can determine the extent of liver fatty changes and scarring, this non-invasive diagnostic approach is often employed in clinical settings for the detection and management of liver diseases.

Only those who were younger than 60, had a history of NAFLD, and were willing to take part in the research were included in it. All the data were input into a computer using SPSS version 27, and a 95% confidence interval was used to determine the percentage of resistance (CI). Prior to analyzing the findings, the team ensured that the statistical significance level was set at a "P" value lower than 0.05 by double-checking it. This research sheds important information on the incidence and risk factors of NAFLD in the local community and emphasizes the need for public health actions to stop and manage this new health concern. The findings of this research will be crucial in helping doctors and health authorities develop successful plans to tackle NAFLD in Pakistan.

RESULTS

Table 1 presents a glimpse into the unique characteristics of the participants of our research study. A large percentage of the participants were in the 40 to 60 age range, making up 51.4% of the total participants, while 48.6% were below 40 years of age. The mean age of the participants was calculated to be 38.89 ± 8.50 years. Notably, 80% of the participants were female, with the majority of them being housewives (68.6%). Additionally, a vast majority of the participants (82.8%) were not accustomed to regular exercise, and 60% of them were classified as middle class based on their socioeconomic status.

Table 2 provides insights into the risk factors present among the participants. It revealed that almost half of the participants

(48.6%) had diabetes mellitus, and 42.9% were diagnosed with obesity. It is noteworthy that none of the participants tested positive for HBs Ag and Anti-HCV. The average body weight and height of the participants were calculated to be 72.74 ± 8.74 and 161.37 ± 2.67, respectively.

Table 1: Participants' demographic information

	Variables	n (%)	Mean ± SD
Age	40-60 yrs.	18(51.4%)	
	<40 yrs.	17(48.6%)	
	Average Age		38.89 ± 8.50
Gender	Female	28(80%)	
	Male	7(20%)	
Exercise	Rice 3 times	19(54.3%)	
	Rice 2 times	13(37.1%)	
	Rice 1 time	3(8.6%)	
Exercise	No	29(82.8%)	
	Yes	5(14.3%)	
	Occasional	1(2.9%)	

Table 2: Participants' status of risk factor

	Variables	n (%)	Mean ± SD
Risk factors	Thyroid disorders	2(5.7%)	
	IHD	2(5.7%)	
	HTN	8(22.9%)	
	Hyperlipidemia	9(25.7%)	
	Obesity	15(42.9%)	
HBs Ag	-ve	35(100%)	
	+ve	0(0%)	
Anti-HCV	-ve	35(100%)	
	+ve	0(0%)	
Body (BMI)	Body Height		161.37 ± 2.67
	Body weight		72.74 ± 8.74

The status of different investigations carried out among the participants is detailed in Table 3. The mean levels of different biomarkers, such as HBA1C, TSH, RBS, ALK PHOS, SGOT, SGPT, S. Bilirubin, and Lipid profiles C, H, L, and T were calculated. Table 3A further elucidates that among the participants, 60% had SGPT levels below 42, while the remaining 40% had SGPT levels above 42.

Table 3: Status of various investigations conducted among the participants

	Variables	Mean	SD	C.I (95%)		P
				Lower	Upper	
Lipid Profile	T	214.54	108.25	177.36	251.73	0.937
	L	120.09	45.91	104.32	135.85	0.137
	H	42.97	10.72	39.29	46.65	0.084
	C	207.14	56.82	187.63	226.66	0.161
	TSH	2.4	1.33	1.94	2.85	0.805
	HBA1c	5.58	1.75	4.98	6.18	0.243
	RBS	6.62	2.99	5.6	7.65	0.231
	ALK PHOS	56.63	24.98	48.05	65.21	0.968
	SGOT	42.94	23.92	34.73	51.16	0.116
	SGPT	50.89	24.82	42.36	59.41	0.011
	S. Bilirubin	0.53	0.2	0.46	0.6	0.544

Table 3A: Participants' SGPT distribution

Variables	SGPT More than 42	SGPT Less than 42
n (%)	14 (40%)	21 (60%)

Table 4 expounds on the hepatic fibrosis status of the participants. A whopping 94.4% of the patients had mild levels of fibrosis, while 5.7% and 2.9% had moderate and severe levels, respectively.

Table 4: Participants' levels of hepatic fibrosis

Hepatic Fibrosis	Stage	Fatty liver score
1-8.6 (Mild)	0,1	32 (94.4%)
8.6-11.7 (Moderate)	2,3	2 (5.7%)
11.7-75 (Severe)	4	1 (2.9%)

Figure 2 depicts the stiffness status of the participants. It showcases the varying levels of stiffness observed among the patients.

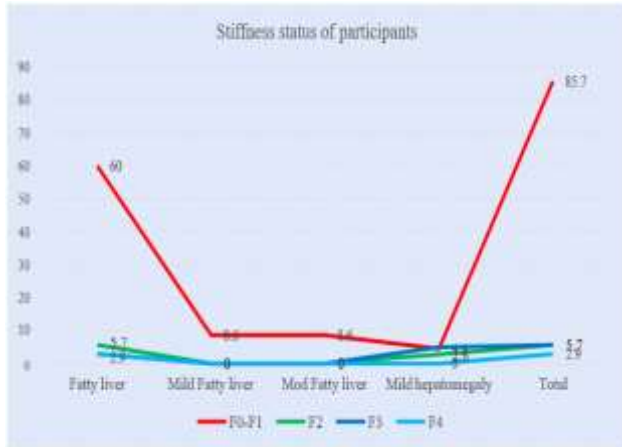


Figure 2: Participants' stiffness status

Table 5 elucidates the hepatic steatosis status of the participants. It reveals that more than half of the participants (57.2%) were classified as stage four severe, while only 11.4% of the participants were classified as mild. The remaining 31.4% of the participants were classified as moderate.

Table 5: Participants' levels of hepatic steatosis

Hepatic steatosis (Fat content in the liver)	Stage	Fatty liver score
1-270 (Mild)	0,1	4 (11.4%)
270-302 (Moderate)	2	11 (31.4%)
302-400 (Severe)	3	20 (57.2%)

Finally, Figure 3 presents the fibro scan status of the participants. The majority of the participants (stage 3) had moderate levels of fibrosis, while the smallest number of participants had stage 1 fibrosis status.

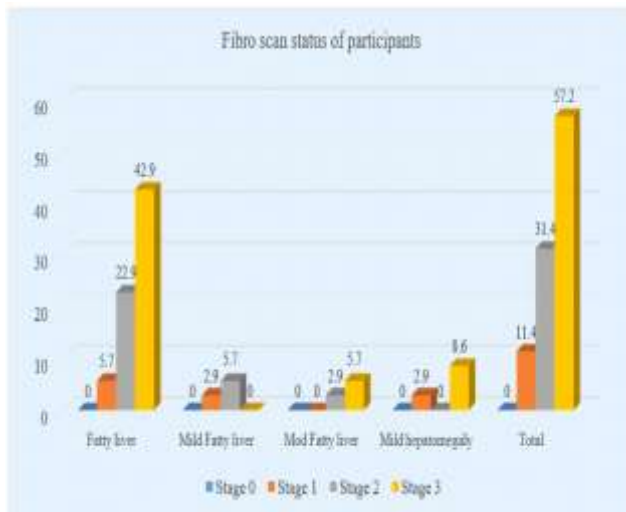


Figure 3: Participants' status of fibro scan

DISCUSSIONS

A large number of people are affected by nonalcoholic fatty liver disease (NAFLD), a common disorder. According to estimates, this condition affects one in three to five persons overall, including one in ten children [9, 10]. Obesity, which was seen in 42.9% of

research participants, as well as diabetes mellitus, which was present in 48.6% of individuals, are the main causes of fatty liver infiltration. The individuals' average body weight and height were 72.74 ± 8.74 and 61.37 ± 2.67 , respectively. According to experts, type 2 diabetes, along with other insulin-resistant conditions like polycystic ovarian syndrome, are well-known risk factors for the development of NAFLD and nonalcoholic steatohepatitis (NASH), which affect approximately two-thirds of obese adults and half of the obese children [11].

It's interesting to note that South Asian research reveals that NAFLD affects young people there, with an average age in their 40s and a greater frequency in men [12,13]. Our study's participants had an average age of 38.89 ± 8.50 years, with 48.6% being under 40 and 51.4% being between 40 and 60.

Like in Western nations, aging, obesity, metabolic syndrome, and insulin resistance are associated with the development of NAFLD in Pakistan [14]. A link between NAFLD and insulin resistance, waist circumference, BMI, and hypertension has been shown in studies on South Asian populations [3]. HOMA-IR, diabetes, waist-hip ratio, HTN, sleep apnea, family history of metabolic syndrome, and specific dietary habits such as non-vegetarian diets, fried foods, spicy foods, and tea intake are additional risk factors for NAFLD in Pakistan [15]. These elements are widespread in Pakistani society and they have a role in the rising prevalence of NAFLD there. Given the growing burden of NAFLD in Pakistan, it is crucial to identify and address these risk factors to prevent and manage the condition effectively. Healthcare providers should prioritize patient education and lifestyle modifications that target weight loss, healthy dietary practices, and regular physical activity to reduce the risk of NAFLD and its associated complications. The elements of the metabolic syndrome were more prevalent in NAFLD patients [16,17]. Moreover, single-nucleotide polymorphisms (SNPs), which are connected to genetic and epigenetic alterations, are among the non-modifiable risk factors for South Asian NAFLD [18].

Less studies have been conducted on the connection between extra metabolic risk variables and incident severe liver disease, and various definitions of pertinent prognostic markers have been used. The findings could not be pooled as a consequence. However, the most comprehensive and high-quality studies suggested that hypertension and lipid abnormalities, such as low levels of high-density lipoprotein (HDL) and high levels of triglycerides, are both independently linked to the occurrence of severe liver disease, with corrected impact sizes that are comparable to those observed in studies of individuals with a high body mass index. Little research has been done on metabolic syndrome, a group of metabolic risk factors, as a predictor of outcomes for the liver [19,20].

CONCLUSIONS

Nonalcoholic fatty liver disease is more common as obesity and type 2 diabetes rates rise, adding to the strain on healthcare systems throughout the globe. To combat this problem, primary care physicians must have a deep understanding of NAFLD, including its risk factors and potential health consequences. This knowledge can help them identify and manage metabolic risk factors in their patients, ultimately reducing the impact of NAFLD on public health.

However, while progress has been made in understanding NAFLD, there is still much that we don't know. We need more population-based research to help us comprehend the intricate interactions of risk variables that cause this illness. Armed with this knowledge, we can develop more effective interventions to prevent and manage NAFLD, ultimately improving the health and well-being of millions of people around the world.

REFERENCES

1. Zamani, M., Alizadeh-Tabari, S., Singh, S., & Loomba, R. (2022). Meta-analysis: prevalence of, and risk factors for, non-alcoholic fatty

- liver disease in patients with inflammatory bowel disease. *Alimentary Pharmacology & Therapeutics*, 55(8), 894-907.
2. Shin, H. S., Hong, M. H., Moon, J. Y., & Sim, S. J. (2022). Periodontal disease could be a potential risk factor for non-alcoholic fatty liver disease: An 11-year retrospective follow-up study. *Clinical Oral Investigations*, 26(8), 5503-5514.
 3. Wang, W., Fan, M., Gong, R., Zhang, Y., Zeng, J., Xu, S., & Lin, R. (2022). *Helicobacter pylori* infection is not an independent risk factor of non-alcoholic fatty liver disease in China. *BMC gastroenterology*, 22(1), 1-10.
 4. Luukkonen, P. K., Qadri, S., Ahlholm, N., Porthan, K., Männistö, V., Sammalkorpi, H., ... & Yki-Järvinen, H. (2022). Distinct contributions of metabolic dysfunction and genetic risk factors in the pathogenesis of non-alcoholic fatty liver disease. *Journal of hepatology*, 76(3), 526-535.
 5. Putri, R. R., Casswall, T., & Hagman, E. (2022). Risk and protective factors of non-alcoholic fatty liver disease in paediatric obesity: A nationwide nested case-control study. *Clinical obesity*, 12(2), e12502.
 6. Stefan, N., & Cusi, K. (2022). A global view of the interplay between non-alcoholic fatty liver disease and diabetes. *The lancet Diabetes & endocrinology*.
 7. Byrne, C. D., & Targher, G. (2022). Non-alcoholic fatty liver disease-related risk of cardiovascular disease and other cardiac complications. *Diabetes, Obesity and Metabolism*, 24, 28-43.
 8. Mantovani, A., Petracca, G., Beatrice, G., Csermely, A., Lonardo, A., Schattnerberg, J. M., ... & Targher, G. (2022). Non-alcoholic fatty liver disease and risk of incident chronic kidney disease: an updated meta-analysis. *Gut*, 71(1), 156-162.
 9. Byrne, C. D., & Targher, G. (2022). Non-alcoholic fatty liver disease is a risk factor for cardiovascular and cardiac diseases: Further evidence that a holistic approach to treatment is needed. *Gut*, 71(9), 1695-1696.
 10. Fresneda, S., Abbate, M., Busquets-Cortés, C., López-González, A., Fuster-Parra, P., Bannasar-Veny, M., & Yáñez, A. M. (2022). Sex and age differences in the association of fatty liver index-defined non-alcoholic fatty liver disease with cardiometabolic risk factors: a cross-sectional study. *Biology of sex Differences*, 13(1), 1-16.
 11. Muthiah, M. D., Cheng Han, N., & Sanyal, A. J. (2022). A clinical overview of non-alcoholic fatty liver disease: a guide to diagnosis, the clinical features, and complications—what the non-specialist needs to know. *Diabetes, Obesity and Metabolism*, 24, 3-14.
 12. Sato, S., Kamata, Y., Kessoku, T., Shimizu, T., Kobayashi, T., Kurihashi, T., ... & Minabe, M. (2022). A cross-sectional study assessing the relationship between non-alcoholic fatty liver disease and periodontal disease. *Scientific reports*, 12(1), 13621.
 13. Pouwels, S., Sakran, N., Graham, Y., Leal, A., Pintar, T., Yang, W., ... & Ramnarain, D. (2022). Non-alcoholic fatty liver disease (NAFLD): a review of pathophysiology, clinical management and effects of weight loss. *BMC endocrine disorders*, 22(1), 1-9.
 14. Zhang, X. L., Wang, T. Y., Targher, G., Byrne, C. D., & Zheng, M. H. (2022). Lifestyle interventions for non-obese patients both with, and at risk, of non-alcoholic fatty liver disease. *Diabetes & Metabolism Journal*, 46(3), 391-401.
 15. Díaz, L. A., Fuentes-López, E., Ayares, G., Idalsoaga, F., Arnold, J., Márquez-Lomas, A., ... & Arab, J. P. (2022). The establishment of public health policies and the burden of non-alcoholic fatty liver disease in the Americas. *The Lancet Gastroenterology & Hepatology*.
 16. Zikiriyayevna, S. G., Makhmudovich, A. S., Fakhridinovich, T. S., & Muxtorovna, E. M. (2022). NON-ALCOHOLIC FATTY LIVER DISEASE. *Web of Scientist: International Scientific Research Journal*, 3(10), 414-422.
 17. Henry, L., Paik, J., & Younossi, Z. M. (2022). the epidemiologic burden of non-alcoholic fatty liver disease across the world. *Alimentary pharmacology & therapeutics*, 56(6), 942-956.
 18. Bonsembiante, L., Targher, G., & Maffei, C. (2022). Non-alcoholic fatty liver disease in obese children and adolescents: a role for nutrition?. *European journal of clinical nutrition*, 76(1), 28-39.
 19. Chrysavgis, L., Giannakodimos, I., Diamantopoulou, P., & Cholongitas, E. (2022). Non-alcoholic fatty liver disease and hepatocellular carcinoma: Clinical challenges of an intriguing link. *World Journal of Gastroenterology*, 28(3), 310.
 20. Rojas, Y. A. O., Cuellar, C. L. V., Barrón, K. M. A., Verdugo, J. P. A., & Miranda, A. L. (2022). Non-alcoholic fatty liver disease prevalence in Latin America: a systematic review and meta-analysis. *Annals of Hepatology*, 100706.