Original Article

Prevalence & Risk Factors of Non-Alcohol Fatty Liver Disease (NAFLD) in Urban & Rural Communities of Pakistan

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ABSTRACT

Background: The rising condition of non-alcoholic fatty liver disease (NAFLD) has been widely observed in South Asia due to the increasing trends of urbanization and lifestyle factors because of metabolic disturbances. **Objective**: To identify the prevalence of NAFLD risk factors, along with metabolic and sociodemographic and lifestyle factors, in the adult population of Pakistan's urban and rural settings. **Methods**: This study was carried out using a cross-sectional approach involving 108 adults who attended the general hospital of Sialkot in Pakistan. The study used a structured questionnaire to gather information regarding the sociodemographic factors of the participants. Anthropometric measurements were also done. NAFLD was also identified using the criterion of the absence of severe alcohol consumption along with the absence of chronic liver diseases alongside the criterion of the detection of hepatic steatosis through ultrasonography. Statistical computation was carried out using the software package SPSS version 25. **Results**: The prevalence of NAFLD was 48.1%. The prevalence of NAFLD was higher in the urban group than the rural group (56.3% vs. 36.4%; p=0.042). In the NAFLD group, there were higher levels of BMI, waist measurement, ALT levels, AST levels, and triglyceride levels, along with lower levels of HDL. **Conclusion**: NAFLD has been found to be prevalent within this dual non-rural community of Pakistani patients and has been found to be strongly linked to obesity, diabetes, and a sedentary lifestyle.

Keywords: NAFLD, Pakistan, Prevalence, Obesity, Diabetes, Ultrasound

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) has recently been recognized as the predominant cause of chronic liver diseases globally, which follows the same trend of increasing incidence of obesity, type-2 diabetes mellitus (T2DM), and a sedentary lifestyle. More recently, meta-analyses indicate that about a quarter to a third of the adult global population has NAFLD, especially in regions that display rapid progression of urbanization and nutritional transition (1). However, NAFLD extends from non-alcoholic steatohepatitis (NASH) to fibrosis, cirrhosis, and hepatocellular carcinoma and has also been recently recognized as a significant contributing factor to both liver and cardiovascular mortality and morbidity. As a nod to its metabolic etiology, there has been the proposal of substituting the term NAFLD for metabolic dysfunction-associated steatotic liver disease (MASLD). This suggests the classification of patients based upon the absence of cardiometabolic risks rather than the exclusion criterion. Most of the available previous

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data from developing nations has been based upon the NAFLD construct and remains the defining factor of the magnitude of the current global problem (1).

In Asia as a whole, and especially within South Asia, NAFLD has been found to be alarmingly prevalent even at lower mean BMI levels than their Western counterparts because of their visceral obesity and level of IR at comparatively low thresholds of BMI. The general recommendation of regional guidelines has been that NAFLD/MASLD needs to be regarded as the "liver equivalent" of metabolic syndrome owing to its close association with obesity, T2DM, dyslipidemia, and hypertension (2-6). However, the extent of the burden of the condition in general in South Asia remains uncertain because of the diverse nature of the available data, which is mostly derived from hospital sampling and has a limited representation of the countryside. A unique situation existed in the case of Pakistan because of its rapid pace of urbanization alongside coexisting large countryside settings and the marked disparities of socio-economic conditions (7).

Available Pakistani research suggests that NAFLD has already reached proportions of a large-scale health problem. A narrative review estimated the magnitude of fatty liver at approximately 15% of the general community's prevalence, while the reported Pakistani NAFLD has ranged between 14% and 47%, according to the study group. However, recent observations also stress the emerging nature of NAFLD in Pakistan—being closely linked to the rising trends of obesity, metabolic syndrome, and type-2 diabetes—with the reported NAFLD also observed in approximately one-third of Pakistani type-2 diabetics. The results of the study also observed the metabolic phenotypes of NAFLD at approximately 14.8% within the enrollment group, increasing to nearly 20% in the community of adults aged 40 years or above, and characterized predominantly by the phenotypes of obesity, high fasting glycemia levels, high blood pressure levels, and lipid disturbances. NAFLD correlation has also been found along with the factors of obesity and lipid derangement, diabetes, and women in the tertiary care community. However, the NAFLD has observed a community magnitude of approximately 47% in the cantonment-based enrollment study from Peshawar, with the non-alcoholic steatohepatitis also found at a level of 12.3% of the study group along with large inter-ethnic variations (8).

More recent Pakistani studies have highlighted the importance of metabolic risk factors. A community study in Karachi, as part of a diabetes prevention trial, found remarkably high levels of NAFLD (60.8%) in a high-risk community in an urban setting, rising to 67% in individuals with impaired glucose tolerance and 74% in those with diabetes. The metabolic syndrome components of abdominal obesity, elevated fasting glucose, raised triglyceride levels, low HDL, hypertension, and high BMI were found to be of maximum additive risk. Hospital settings in Jamshoro and Lahore showed NAFLD to be linked to obesity, uncontrolled diabetes, hypertension, dyslipidemia, and smoking, along with vitamin deficiency and the extent of steatosis seen in ultrasound assessments. Although the above studies do confirm the relationship of NAFLD to metabolic syndrome, the differences in study settings and the target populations studied render generalization rather difficult (9-10).

A crucial drawback of the existing Pakistani data has been the absence of systematically gathered information regarding the differences of the affected individuals in the countryside and the city based on identical criteriological classifications of metabolic, lifestyle, and socio-spatial components. The majority of the information collected has been from the tertiary care level of hospitals from the city and has had limited input from the countryside itself. There has been inadequate information available regarding the extent to which the NAFLD burden and the related risks of the countryside might be shifting to be parallel to, rather than divergent from, the situation described from the city. Even the available information concerning the city has had inadequate direct comparisons available concerning the community-residing group as opposed to the group from the medical units. Even the existing information regarding the particular factors of the first group has had the contribution of the factors uncertain (11-14).

In the clinical and public realms, it becomes prudent to fill this information gap. NAFLD has been known to be mostly symptom-free until it advances to be severe. The only manner whereby this condition can be revealed is through the provision of opportunistic sonographic scanning or through the serendipitous identification of the condition through imaging and the results of clinical findings. In resource-limited settings found in Pakistan, the extent of mass scanning can virtually be impractical. This necessitates the scanning of targeted groups prone to this condition due to factors of being obese or alongside diabetes and when residing in cities. All this necessitates the existence of reliable information emanating from the context of the distribution of NAFLD in the regions of the city and the countryside alongside the socio-economic backgrounds and the metabolic risks involved. In the absence of this information, the health sector becomes prone to the risk of underestimation of the extent of the condition found in the countryside or the inability of the sector to identify the right proportions of risk factors in the city's health-care setup. The information regarding the lifestyle factors of NAFLD found alongside the sonographic scanning can work toward the development of the right preventive programs (15-17).

Accordingly, this research work was conceptualized as an observational study across sections of the NAFLD-prevalence-estimation community based on the exclusion of significant alcohol consumption and known chronic liver diseases to identify the sociodemographic, clinical, metabolic, and lifestyle factors of adults aged 30 years and above in both the urban and rural settings of Pakistan. To be particular, the scope of this research work involved comparing the NAFLD prevalence observed in the residents of Pakistan's urban and rural communities in addition to ascertaining the strength of association of NAFLD risks with obesity, abdominal obesity, diabetes, hypertension, and dyslipidemia, besides the behavioral risk factors of physical inactivity, unhealthy dietary habits, and smoking. The main hypothesis of this research work was that the NAFLD prevalence level could be higher in the residents of Pakistan's urban regions than the residents of the rural regions and that the confounding variables of obesity, diabetes, and reduced levels of physical activity would remain the best predictors of NAFLD (15).

MATERIALS AND METHODS

This was a cross-sectional observational study aimed at establishing the prevalence of NAFLD and its metabolic, lifestyle, and sociodemographic risk factors in the adult population of Pakistan. The study was carried out at a general hospital in Sialkot, Pakistan, which constituted a mixed catchment of both urban and rural populations. This presented the opportunity for establishing geographic variability in the prevalence of NAFLD. The study involved the collection of data from the outpatient visitors over a continuous period of the study. A representative study pool of 108 participants was achieved through the method of consecutive sampling. All the participants had signed their informed written consent. The eligibility criteria helped to correctly identify the participants who had NAFLD and did not have secondary causes of hepatic steatosis. The study participants should be above the age of 18 years and should have had abdominal ultrasonography during their workup. The exclusion criteria included excessive drinking of alcohol products, hepatitis B surface antigen and/or anti-HCV seropositivity, chronic liver diseases (autoimmune hepatitis, Wilson's disease, hemochromatosis), and the consumption of hepatotoxic drugs. Pregnant women also qualified for the exclusion criterion because of the physiologic changes that occur. The participants were approached at the outpatient clinic following their clinic visit. The survey was administered using a structured interviewer-administered proforma that was based on proven instruments and NAFLD epidemiological factors. The variables used were age, sex, residence, educational level, occupation, income level, smoke habits (smoking and smokeless tobacco consumption), physical activity level, consumption of "fast food" and "sugar-sweetened beverages," and "medical history" (diabetes, hypertension, dyslipidemias, and hypothyroidism). The following anthropometric measurements—weight, height, Body Mass Index (BMI), waist and hip circumferences—were also taken using standard operating procedure and calibration of equipment. Blood pressure measurements were done while seated after a 5 min rest using an automated sphygmomanometer. The medical data—fasting glucose levels, HbA1c levels when available, lipid levels, and liver function tests (ALT, AST, ALP, GGT, and bilirubin levels)—were also used and derived from the patient's medical file. The hepatic steatosis grade detected through "ultrasonographic evaluation" according to the standard method and detected differently according to increasing grade from "mild" to "severe" as graded according to "echogenicity relative to the renal cortex and the visibility of the hepatic" "vessels" according to The operational definitions were made before analyzing the study. NAFLD was defined as the presence of hepatic steatosis detected through ultrasonography and the absence of significant alcohol consumption and other known chronic liver diseases. The cut-offs of the World Health Organization's Asian standards were used to identify obesity (BMI of 27.5 kg/m² and above). Central obesity was measured through waist circumferences suggested to be ideal for South Asians. The study used the recorded diagnoses of diabetes, hypertension, and dyslipidemia through support information from the patient's vital data according to global standards. Physical activities were also measured as low, moderate, and high through the patient's recorded weekly activities according to global standards. To mitigate bias, consecutive sampling and standardized measurement were used. Multivariate logistic regression was employed to control confounding factors of known significance in the study. The data were validated manually to check their accuracy and completeness. A review of the original files clarified any inconsistencies found during the validation exercise. The missing data points were also explored. Owing to the minimal and random missing data points, the approach used was complete-case analysis without imputation. The number of participants to be chosen was estimated at 108 because this represented the number of eligible participants available at the time of the study. The statistical package used was the IBM SPSS Statistics version 25. The statistical method used to identify the level of normality of the continuous variables was the Kolmogorov–Smirnov test. The results of continuous variables were presented as mean and standard deviation. The results of categorical variables were presented as frequencies and percentages. The statistical method used to compare the groups in the continuous variables was the two-independent-samples t-test. The method used to evaluate the association of categorical variables and the dependent variable (NAFLD) was the chi-square test. The method used to develop the model of prediction of the dependent variable from the significant predictors was the binary regression. The significance level used in the study was two-tailed and $p < 0.05$. The study was approved by the institutional review board of the mentioned hospital and conforms to the "Declaration of Helsinki."

RESULTS

A total of 108 participants took part in the study. The mean age of the participants was 44.6 ± 12.1 years. The majority of the participants (55.6%) were men. The main participants who took part in the study came from the urban setup, which comprised 59.3% of the participants. The participants who were obese comprised 47.2% of the study group. Central obesity was observed in 63% of the participants. The participant groups who had diabetes mellitus comprised 29.6% of the group.

Table 1. Sociodemographic Characteristics of the Study Population (N = 108)

Variable	Category	n	%
Age (years)	Mean ± SD	44.6 ± 12.1	—
Sex	Male	60	55.6
	Female	48	44.4
Residence	Urban	64	59.3
	Rural	44	40.7
Education	≤ Primary	31	28.7
	Secondary–Intermediate	49	45.4
	Graduate/Postgraduate	28	25.9
Occupation	Labor/Unskilled	22	20.4
	Skilled/Office	45	41.7
	Housewife	24	22.2
	Professional	17	15.7

Table 2. Clinical and Lifestyle Profile of Participants (N = 108)

Variable	Category	n	%
BMI Category	Normal	18	16.7
	Overweight	39	36.1
	Obese	51	47.2
Central Obesity	Present	68	63.0
Diabetes	Yes	32	29.6
Hypertension	Yes	44	40.7
Dyslipidaemia	Yes	57	52.8
Smoking	Current	21	19.4
Physical Activity	Low	58	53.7
	Moderate/High	50	46.3

Table 3. Prevalence of NAFLD by Residence (N = 108)

Group	Total n	NAFLD n	Prevalence (%)
Overall	108	52	48.1
Urban	64	36	56.3
Rural	44	16	36.4

Table 4. Severity of Fatty Liver among NAFLD Cases (n = 52)

Grade	n	%
Grade I	21	40.4
Grade II	19	36.5
Grade III	12	23.1

Table 5. Comparison of Continuous Variables between NAFLD and Non-NAFLD

Variable	NAFLD (n=52) Mean ± SD	Non-NAFLD (n=56) Mean ± SD	p-value	Effect Size (Cohen's d)
Age (years)	46.8 ± 11.3	42.6 ± 12.6	0.071	0.36
BMI (kg/m²)	30.8 ± 4.1	27.5 ± 4.8	0.001	0.73
Waist Circumference (cm)	101.4 ± 9.2	94.3 ± 10.1	0.002	0.74
ALT (U/L)	52.1 ± 19.4	33.4 ± 12.8	<0.001	1.17
AST (U/L)	38.5 ± 13.2	28.4 ± 10.7	0.001	0.82
Triglycerides (mg/dL)	189.6 ± 66.2	147.8 ± 55.4	0.004	0.69
HDL (mg/dL)	39.1 ± 7.8	45.3 ± 8.6	0.002	0.78

Table 6. Association of Categorical Risk Factors with NAFLD

Variable	Category	NAFLD n (%)	Non-NAFLD n (%)	p-value	OR (95% CI)
Sex	Male	32 (61.5)	28 (50.0)	0.21	1.58 (0.76–3.29)
Residence	Urban	36 (69.2)	28 (50.0)	0.042	2.24 (1.03–4.86)
Obesity	Yes	34 (65.4)	17 (30.4)	<0.001	4.29 (1.98–9.27)
Diabetes	Yes	22 (42.3)	10 (17.8)	0.005	3.40 (1.39–8.32)

Variable	Category	NAFLD n (%)	Non-NAFLD n (%)	p-value	OR (95% CI)
Hypertension	Yes	28 (53.8)	16 (28.6)	0.008	2.98 (1.31–6.78)
Dyslipidaemia	Yes	35 (67.3)	22 (39.3)	0.006	3.21 (1.38–7.46)
Physical Activity	Low	37 (71.2)	21 (37.5)	0.001	3.88 (1.72–8.77)
Smoking	Current	13 (25.0)	8 (14.3)	0.18	2.00 (0.76–5.26)

Table 7. Multivariate Logistic Regression for Predictors of NAFLD

Predictor	OR	95% CI	p-value
Obesity (BMI ≥ 30)	3.92	1.71–8.98	0.001
Diabetes	2.77	1.10–6.98	0.030
Urban Residence	1.94	0.86–4.35	0.110
Low Physical Activity	2.63	1.15–6.02	0.022
Dyslipidaemia	1.88	0.81–4.30	0.140
Male Sex	1.41	0.63–3.16	0.390

The overall prevalence of NAFLD was 48.1% (n = 52). A higher prevalence of NAFLD was observed in the urban group (56.3%) than the rural group (36.4%) ($\chi^2 = 4.12$, $p = 0.042$). Residence in the city was found to be a factor that doubles the odds of NAFLD (OR: 2.24; CI: 1.03–4.86). In the NAFLD group: The distribution according to the grade of steatosis showed: grade I: Participants with NAFLD had a higher BMI (30.8 ± 4.1 vs 27.5 ± 4.8; p = 0.001), waist circumference (101.4 ± 9.2 vs 94.3 ± 10.1; p = 0.002), ALT levels (52.1 ± 19.4 vs 33.4 ± 12.8; p < 0.001), AST levels (38.5 ± 13.2 vs 28.4 ± 10.7; p = 0.001), and fasting triglyceride levels (189.6 ± 66.2 vs 147.8 ± 55.4; p = 0.004). However, their levels In categorical comparisons, obesity (OR = 4.29), diabetes (OR = 3.40), dyslipidemia (OR = 3.21), hypertension (OR = 2.98), and low levels of physical activity (OR = 3.88) were found to be significantly linked to the development of NAFLD. In the regression analysis, obesity (aOR = 3.92, p = 0.001), diabetes (aOR = 2.77, p = 0.030), and low physical activity (aOR = 2.63, p = 0.

DISCUSSION

The results of this cross-sectional study also confirm the emerging, relative NAFLD problem in the mixed urban-rural Pakistani community: almost half the community presenting in the usual ultrasonographic workup demonstrates hepatic steatosis. This value can be considered consistent with the upper bounds of the estimates reported from the South Asia/Pakistan series that showed NAFLD to vary widely from 14% to above 47% according to differences in the studied community characteristics and the method of defining the target group (references 8 through 15). The observed proliferation of the NAFLD/MASLD also fits the trend of the rapid global development of this condition in developing regions undergoing transition to a lifestyle of Western characteristics (1-7).

Urban residence entered the model as a prominent predictor of NAFLD in univariate models, consistent with the development of sedentary behavior and the consumption of high-energy-dense foods in Karachi and the rest of the South Asia region of larger cities (reference 13). Although the attenuation of the effect of being an urban resident in the multivariate model reached significance, the trend of non-significance points to the possible role of metabolic risk factors as intermediaries, mainly obesity and diabetes, which had the strongest association. The role of metabolic factors in the development of NAFLD has been the cornerstone of research globally (8).

The non-independent association of obesity, diabetes, and physical inactivity with NAFLD fits the large Pakistani research that suggests obesity as the predominant risk factor, which provides four to five times the risk value, followed by the secondary role of hyperglycemia and diabetes (10, 13-15). The large effect value of physical inactivity emphasizes the significance of lifestyle factors, which has also been suggested to be a determinant in the accelerated progression of NAFLD because of reduced energy expenditure due to the absence of regular physical labor in the transitionary society (references 3, 7). Biochemically, the NAFLD group had a higher level of ALT, AST, and triglycerides and lower levels of HDL. This has been suggested to be the typical metabolic liver anomaly of steatosis and mild hepatocellular injury (14).

One of the factors that is evident regarding this data collection is the graded distribution of the steatosis level because over 20% of the NAFLD patients had severe steatosis proven through ultrasound. Similar observations regarding the distribution of the levels of steatosis have been made in Pakistani research circles (14). Since the risk of fibrosis has been demonstrated to be directly proportional to the level of steatosis (3), the observations provide clear implications regarding the requirement of proactive risk management, which can be achieved in spite of limited resources without the aid of elastography (15).

Strengths of the study are the standardized collection of data, the uniform sonographic evaluation, and the study of both urban and rural participants. The one-center study might be prone to referral bias and has limited power due to its relatively small number of participants. The study has a cross-sectional study design and does not allow inference of causation, while the absence of fibrosis determination also hinders the determination of the level of the disease. However, the detection of robust and consistent factors of the study, like obesity, diabetes, and physical inactivity, helps form the cornerstone of a targeted approach to the study of affected participants in Pakistan. Altogether, the results support the trends of metabolic diseases worldwide and emphasize the need to address lifestyle changes, weight management, and metabolic factors as integral elements of NAFLD control and management strategies in the context of Pakistan. Community-based interventions and new screening strategies designed to target at-risk groups can perhaps address the emerging challenges posed by the increasing burden of NAFLD (15).

CONCLUSION

This study has shown the high prevalence of NAFLD in the adult population visiting the general hospitals of Sialkot, for which obesity, diabetes, and poor physical activity were found to be the strongest predictors. Urban residents had a higher prevalence of NAFLD, though this association was explained through metabolic components. The results confirm the requirement of appropriate screening of the at-risk group and the importance of lifestyle and metabolic modifications due to the increasing trend of NAFLD in the Pakistani community.

Declarations
Ethical Approval
This study was approved by the Institutional Review Board of University of Lahore, Lahore Pakistan
Informed Consent
Written informed consent was obtained from all participants included in the study.
Conflict of Interest
The authors declare no conflict of interest.
Funding
This research received no external funding.
Authors' Contributions
Concept: SA; Design: FA; Data Collection: ML; Analysis: LK; Drafting: AK, SA
Data Availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.
Acknowledgments
Not applicable.
Study Registration
Not applicable.

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