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Ultrasound Detected Non-Alcoholic Fatty Liver Disease Prevalence and its Risk Factors in Pakistani Population

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Abstract

Background: Nonalcoholic fatty liver disease (NAFLD) is the most common predictor of chronic liver disease. It is an emerging health condition in Pakistan and in most cases, the disease remains undiagnosed due to a low trend of screening processes observed over the years. The purpose of this research was to assess the relationship of ultrasonography (USG) – detected NAFLD with the risk factors including obesity, diabetes, hypertension, and menopause.

Methods: This cross-sectional study evaluated the data gathered from medical histories, anthropometric measurements, and diagnostic abdominal ultrasound scans of 87 patients referred to radiology department of a trust hospital in Lahore, Pakistan. Patient diagnosed with NAFLD without any other disease or complication were selected through purposive sampling for further study.

Results: The results depicted a higher prevalence of NAFLD in females. Among diagnosed NAFLD patients, most (33.7%) showed signs of mild fatty liver on USG. Statistically, a significant (p value= 0.002) relationship of obesity with NAFLD was observed. NAFLD patients had higher mean BMI values (31.04 ± 4.67 Kg/m^2, p value = 0.000) as compared to other patients (25.34 ± 4.71 Kg/m^2), confirming that obesity is the most important risk factor for NAFLD. Other risk factors (diabetes, hypertension, and menopause) were not found to be significantly related to NAFLD.

Conclusion: The major finding of this study is that higher BMI increases the likelihood of developing NAFLD. Prevention and treatment of overweight and obesity can reduce the prevalence of NAFLD.

Introduction

Fatty liver disease (FLD) is the triglycerides buildup in the hepatocytes and is called nonalcoholic fatty liver disease (NAFLD) in the absence of alcohol consumption [1,2]. NAFLD is asymptomatic but may present with vomiting, nausea, fatigue, itching, generalized weakness, pain and fullness in right upper abdomen. About 30% of liver steatosis can be detected through imaging modalities. Increased echogenicity and Hepatomegaly are the signs associated with NAFLD seen on ultrasonography (USG) [3]. The presence of NAFLD is linked with gender and age and has proven association with diabetes mellitus, hypertension, dyslipidemia, and hyperuricemia.[4] Moreover, patterns of dietary changes also play a significant role in the development of FLD [3,5]. Increasing burden of obesity along with metabolic diseases in the Pakistani population is a possible cause of NAFLD [6]. If left undiagnosed or untreated, it can lead to liver cirrhosis and hepatocellular carcinoma [7]. According to an epidemiological study, 25.24% of the world population suffer from NAFLD [8]. A local study reported a higher prevalence in Pakistani diabetic females than diabetic males (62.75% vs 37.25%) detected through ultrasound [3,5]. NAFLD is most commonly observed in the age group of 40 - 60 years [9]. Following menopause, hepatic ability to oxidize fatty acids is reduced, having an inverse relation with lipogenesis leading to excessive hepatic fat deposition and hepatic inflammation in the females; a major stimulus for the acquisition and progression of NAFLD [1]. The inappropriate eating patterns and reduced physical activity are always consistent in the worldwide prevalence of this disease. Obese individuals are more likely to develop fatty liver as compared to normal weight individuals [2]. Adipose tissue dysfunction in obesity and diabetes mellitus, hinders the glucose and lipid metabolism by secreting a large number of fat-derived cytokines and ectopic fat deposition, leading to lipotoxicity and NAFLD [10-12].

There is limited data available on the prevalence of NAFLD in the Pakistani population. Considering it as an emergent problem in Pakistan, sufficient evidence is needed regarding factors that increase the risks of this disease. Non – invasive screening of large populations for NAFLD can be done through diagnostic ultrasound as it is non-ionizing, cost-effective and widely available [2,6]. Aim of this study is to investigate the risk factors associated with the prevalence of NAFLD detected through ultrasonography in Pakistani population.

Methods

This is a cross-sectional and correlational study to find the prevalence of nonalcoholic fatty liver disease in both genders and its relationship with obesity, diabetes, gender and hormonal changes using ultrasonography. The study was performed in Radiology department of a Surayya Azeem Trust Hospital in Lahore, Pakistan from 2018 to February 2019. Purposive sampling technique was used to collect data from 87 abdominal ultrasound participants referred to radiology department during the study period. Patients between the ages 20 to 75 years with no alcohol consumption were included in the study. Pregnant females, patients with viral hepatitis and confirmed or suspected liver pathologies or undertaking liver medications were excluded from the study. Verbal informed consent was taken from every subject. Interviewer administered questionnaire was used to ask question from each participant prior to the ultrasonography exam, which included the information regarding age, present medical condition, past medical history of diabetes mellitus and hypertension, alcohol consumption and menstrual history in case of female participants. Body mass index (BMI) of all participants was calculated by measuring the height (meters) and weight (kilograms). Asian BMI cutoff values were used to categorize subject into underweight (BMI<18.5 kg/m^2), normal weight (BMI=18.5-23 kg/m^2), overweight (BMI=23-24.9 kg/m^2), pre obese (BMI=25-29.9 kg/m^2), obese (BMI=30-40 kg/m^2) and morbid obese (BMI>40.1 kg/m^2) [13]. Females with no menstruations for 12 consecutive months were categorized as menopausal.

High resolution B mode ultrasonography on machine model Mindray logic 6, having a convex and curvilinear transducer of 3.5-5 MHz frequency was used. Liver was examined in parasagittal, inter-coastal and subcoastal scan planes to view liver – kidney contrast, middle and right hepatic vein and left lobe to right lobe from superior to inferior views respectively in supine position. Diagnostic criteria for fatty liver through ultrasonography was defined as hyperechoic hepatic echogenicity as compared to renal echogenicity, decreased (blurring) or no visualization of hepatic vessels or diaphragm, unusual hepatic texture and hepatomegaly (liver size > 17 cm) [2].

According to radiological imaging fatty liver is further classified into 3 grades based on its severity. Grade I- mild fatty liver, mild increase in hepatic echogenicity, same as that of renal cortex with normal visualization of diaphragm and hepatic vascularity. Grade II- moderate fatty liver, moderate rise in hepatic echogenicity with decreased visualization of diaphragm and intrahepatic vessels. Grade III- severe fatty liver, well-defined marked hepatic echogenicity with minimal or no visualization of diaphragm and hepatic vascularity [1,14]. Statistical analysis was performed by using IBM SPSS Statistics 21, Version 21.0. Data of continuous and categorical variables was described as Mean ± SD and frequency (percentages) respectively. Inferential statistics including chi-square test and t-test was used.

Statistical testing was performed at 95% confidence interval with $p<0.05$ taken as significant.

Results

A sample size of 87 participants with age group 20 - 75 years was selected for this study. 61 (70.1%) females and 26 (29.9%) males with mean age and BMI of 42.08 ± 14.94 years and 27.89 ± 5.75 kg/m^2 respectively, were screened through an abdominal ultrasound for the detection of NAFLD. Out of 36(41.37%) participants who screened positive for NAFLD, most (29(33.3%)) showed mild fatty changes in the liver (Grade I), whereas only 7 (8%) participants showed the signs of moderate fatty liver (Grade II). Data gathered for the determinants of NAFLD showed that 25 (28.7%) participants had hypertension, 10(11.5%) had diabetes mellitus and 21(34.4%) female participants were menopausal as shown in Table 1.

Variables		Mean ± SD	Frequency (Percentage)
Age (years)		42.08 ± 14.94	-
BMI (Kg/m^2)		27.89 ± 5.75	-
Gender	Female	-	61 (70.1%)
	Male	-	26 (29.9%)
Study Participants		-	
Normal Participant (without NAFLD)		-	51 (58.6%)
NAFLD Grade I		-	29 (33.3%)
NAFLD Grade II		-	7 (8%)
Hypertension		-	25 (28.7%)
Diabetes mellitus		-	10 (11.5%)
Menopausal female (N=61)		-	21 (34.4%)

Table 1: Prevalence of hypertension and diabetes mellitus in study population

The relationship between BMI and the prevalence of NAFLD is summarized in table 2. All of the participants were divided into different categories based on their BMI values. Most participants falling into the category of underweight (5(100%)), normal weight (12(92.3%)), overweight (6(85.7%)) and pre-obese (18(54.5%)) did not show any signs of fatty liver disease. However, 17 (65.4%) obese and 1 morbidly obese (100%) participant were diagnosed with NAFLD. Chi- square test showed that, obese and morbidly obese participant with the BMI ⩾ 30.0 Kg/m^2 have statistically (p value= 0.002) higher prevalence of NAFLD. Results of the T-test showed that the patients with NAFLD had statistically significant (p value = 0.000) higher mean BMI values (31.04 ± 4.67 Kg/m^2) as compared to the participants with normal liver (25.34 ± 4.71 Kg/m^2) on ultrasound examination proved.

Table 3 shows the impact of risk factors on the prevalence of NAFLD. On ultrasound detection, more (27(44.3%)) female were diagnosed positive for NAFLD as compared to male (9(36%)). Among 25 hypertensive patients, 52% screened positive, whereas half (50%) of the diabetic patients reported the changes of fatty liver. Out of 21 menopausal females, 11 (52.4%) fulfilled the criteria of having NAFLD. But this difference in the higher prevalence of NAFLD in hypertensive, diabetic and menopausal female is not statistically significant.

Variables		Frequency (Percentages)		Chi-square test	p value
		Normal	Nonalcoholic fatty liver disease		
BMI categories	Under weight	5(100%)	0(0%)	19.576	0.002
	Normal	12(92.3%)	1(7.7%)		
	Overweight	6(85.7%)	1(14.3%)		
	Pre obese	18(54.5%)	15(45.5%)		
	Obese	9(34.6%)	17(65.4%)		
	Morbid obese	0(0%)	1(100%)		
BMI values (Kg/m^2)		Mean ± SD		T test	p value
		Normal	Nonalcoholic fatty liver disease		
		25.34 ± 4.71	31.04 ± 4.67	-5.508	0.000

Table 2: Association of obesity with nonalcoholic fatty liver disease in study population

Variables		Frequency (Percentages)		p value
		Normal	Nonalcoholic fatty liver disease	
Gender	Female	34(55.7%)	27(44.3%)	0.481
	Male	16(64%)	9(36%)	
Hypertension		12(48%)	13(52%)	0.222
Diabetes mellitus		5(50%)	5(50%)	0.579
Menopausal female		10(47.6%)	11(52.4%)	0.505

Table 3: Risk factors associated to nonalcoholic fatty liver disease in study population.

Discussion

NAFLD is asymptomatic, the chances of it being diagnosed are very low but with the rapid urbanization, sedentary lifestyle leading to reduced physical activity and use of high fat diet, the prevalence of obesity, diabetes, hypertension and hormonal changes have increased tremendously and this in return increase the chances of developing NAFLD [2,6,15]. From previous studies, the prevalence of USG-detected NAFLD was noted to be 24.13% from USA, 23.17% from Europe, 18.45% from Japan, 17.2% from China [13]. In comparison with these developed countries, our research on Pakistani population suggests higher prevalence of USG-detected NAFLD in 41.37% of the study population.

Gender is considered as major determinant of fatty liver disease. Male gender is more prone toward developing NAFLD than females [1]. According to 3rd National Health and Nutrition Examination Survey (NHANES) most studies showed significantly increased incident of NAFLD in males as compared to females [16]. William *et al.*, studied the influence of gender differences in the prevalence of NAFLD and found higher incidence in males than females (54.4% and 34% respectively, p=0.0370) [17]. Same was observed in much other research [15,16]. Gender differences are due to the low level of estrogen and androsterone in males in comparison to pre-menopausal females who have more estrogen which inhibit the progression of fatty liver. However, females with post-menopausal stage with age more than 50-60 years have low level of estrogen and

androsterone. This may suggest that female hormones have some influence on lipid metabolism and development of fatty liver [15]. But in this research although not significant yet females had higher percentage (44.3%) of fatty liver as compared to male (36%) on examination. The possible reason is because 34.4% of the females included in this study were menopausal that resulted in the higher prevalence is female population. Taseer *et al.*, also found higher prevalence of NAFLD in Pakistani diabetic females (62.75%) than diabetic males (37.25%) with mean age of 47.93 ± 8.57 years [3]. Metabolic or hormonal changes in female body after the menopause are the major stimulus for the progression and acquisition of NAFLD [18].

Insulin resistance causing the diabetes mellitus (type 2) is one of the factors that accumulates free fatty acid load in the liver, as a result liver secretes very low-density lipoprotein that are rich in triglycerides. Hypertriglyceridemia is a character of metabolic syndrome which has strong influence on NAFLD [19]. Similar mechanisms can also be found in obese patients [20]. Irregularities in nutrition and appetite, high intake of energy dense foods and reduced physical activity are lifestyle factors responsible for NAFLD. According to Lim *et al.*, numerous changes in industrial and socioeconomic factors have led to an increased risk of developing many non–communicable diseases like cardiovascular diseases, hypertension, and metabolic diseases like insulin resistance, diabetes mellitus, hyperlipidemia, and NAFLD through overeating and sedentary lifestyle. The link of obesity with non–communicable diseases make it, an important risk factor [21]. Likewise, this study also suggests that prevalence of NAFLD in obese participants is significantly (p value= 0.002) higher as compared to individuals with normal BMI. The findings of another study on Pakistani population are in line with our results, in which 43 obese patients (BMI > 30 kg/m^2) out of 45 were diagnosed with fatty liver [22]. The impact of higher BMI score and obesity in the development and prognosis of NAFLD was found to be statistically significant (p value = 0.00) and all other possible risk factors including gender, diabetes mellitus, hypertension and menopause were not significantly influencing the frequency of fatty liver in this particular study population.

The increased prevalence of obesity and other metabolic diseases in the Pakistani population implicate that the population is at high risk of developing NAFLD, as proposed by the present evidence. Therefore, it is much needed to identify the population at risk and devise strategies for successful screening of individuals in a routine ultrasound scan to prevent its progression to chronic liver disease.

Competing Interest

The authors declare that there is no conflict of interest.

Author Contributions

Muzna Waseem: Idea and design of study, data collection, ultrasonography and write up of manuscript.
Fizza Saeed: Idea and design of study, data collection, ultrasonography and write up of manuscript.
Rida Khan: Data analysis, formatting, and review of manuscript.

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