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Original Article

Frequency of Liver Fibrosis by Non-Invasive Marker in Patients with Non-Alcohol Fatty Liver Diseases

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ABSTRACT

Nonalcoholic fatty liver disease (NAFLD) is one of the most important causes of liver disease. NAFLD is commonly associated with obesity, insulin resistance and other metabolic abnormalities such as hypertriglyceridemia and hyperuricemia. Patients with NAFLD can be properly rationalized and with early exploration and management of fatty liver the progression and complications of NAFLD in relation to liver fibrosis can be reduced on priority basis because the APRI is noninvasive and a simple calculation of two laboratorial variables. **Objective:** To determine the frequency of liver fibrosis by non-invasive marker in patients with non-alcohol fatty liver disease. **Methods:** This cross-sectional descriptive study was conducted upon 164 patients with NAFLD, presented at Department of Medicine, Liaquat University Hospital, Hyderabad. All the patients with NAFLD were evaluated and explored for liver fibrosis through APRI by taking 2cc venous blood sample in a sterilized syringe by principal investigator and send to laboratory for analysis to get the AST and platelet count. An APRI score greater than 0.7 was set cut off for significant hepatic fibrosis. The data were collected on pre-designed proforma. The study lasted 6 months from 26th February 2020 to 31st August 2020. **Results:** The mean age of the patients was 48.15±11.13 years. Frequency of liver fibrosis by non-invasive marker in patients with non-alcohol fatty liver disease was 10.98% (18/164). The mean APRI score was found to be 1.8±0.6. **Conclusions:** It was concluded that APRI is noninvasive and a simple calculation of two laboratory variables and can easily be used at the bedside or in an outpatient setting to assess the liver fibrosis. In this way, the management of NAFLD can be improved.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is one of the most important causes of liver disease worldwide and will likely emerge as the leading reason of end stage liver disease in the near future thus placing a growing strain on health-care systems [1, 2]. It has a global prevalence of 24% and involves a high risk of liver-related morbidity and mortality along with metabolic comorbidities and covers a wide spectrum of histologic lesions, ranging from isolated hepatic steatosis (NAFLD) to nonalcoholic steatohepatitis (NASH), the latter characterized by the presence of lobular inflammation and hepatocyte ballooning with or without fibrosis [3-5]. NAFLD is commonly associated with obesity and insulin resistance which per se are closely related to a cluster of other metabolic abnormalities such as hypertriglyceridemia and hyperuricemia [6]. As per World Gastroenterology Organization Global Guidelines the NAFLD prevalence rate in general Pakistani population is 18% [7]. A number of small population-based studies have reported general as well as gender specific NAFLD frequency rates and disease risk factors [8, 9]. As globally declared the alarmingly increasing frequency of NAFLD could be a manifestation of gradual rise in overweight / obesity along with common metabolic health complications [10]. Literature has determined that the

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addition of established simple markers augmented the diagnostic performance and that liver biopsy could be avoided in 88% of cases [11]. The aspartate aminotransferase-to-platelet ratio index (APRI) score has been validated in patients with chronic liver disease [12]. The prevalence for liver fibrosis through APRI in NAFLD is 15% [13]. The major question addressed in present study was to explore the susceptibility of Pakistani population towards existence of liver fibrosis in NAFLD through simple noninvasive markers, to which the study was aimed to determine the accuracy of Non Invasive Marker (APRI) in diagnosis of Liver Fibrosis among NAFLD patients by measuring frequency of liver fibrosis by non-invasive marker in patients with Non-alcohol fatty liver disease.

METHODS

This cross-sectional descriptive study was conducted upon 164 patients with NAFLD, presented at Department of Medicine, Liaquat University Hospital-Hyderabad. All the patients with NAFLD were evaluated and explored for liver fibrosis through APRI by taking 2cc venous blood sample in a sterilized syringe and send to laboratory for analysis to get the AST and platelet count. An APRI score greater than 0.7 was set cut off for significant hepatic fibrosis. The sample size was calculated by WHO open epi calculator via taking prevalence of liver fibrosis by non-invasive marker (APRI > 1.0) in non-alcoholic fatty liver diseases as 4% with margin of error as 3% and confidence interval of 95%. The patients with NAFLD for = 6 weeks duration not taking any treatment, of 20-60 years of age and either gender were included in the study while the patients having history of daily alcohol consumption (evaluate on history), patients taking corticosteroids, immune-suppressive therapy and lipid-lowing agents or patients of known cases of chronic liver diseases as chronic viral hepatitis or autoimmune hepatitis, malabsorption syndrome and chronic renal failure and the pregnant and lactating ladies were excluded from the study The data were collected on pre-designed proforma. The data of all patients were analyzed in SPSS version 20.00. The frequency and percentage were calculated for gender and residence (urban or rural), hypertension, smoking, obesity (BMI), diabetes mellitus, hyperlipidemia, hypomagnesemia, hyperuricemia and diabetes mellitus and liver fibrosis. The study lasted 6 months from 26th February 2020 to 31st August 2020.

RESULTS

There were 164 patients with NAFLD included in this study. The mean age of the patients was 48.15±11.13 years and duration of NAFLD was 10.32±2.93 week and other demographic are also reported in Table 1. The mean APRI score was found to be 1.8±0.6. There were 77 (46.95%) males and 87(53.05%) females(Table 1).

Variables	Mean ± SD / N (%)
Age (Years)	48.15±11.13
Duration Of NAFLD (Weeks)	10.32±2.93
Weight (Kg)	58.84±10.11
Height (Cm)	162.64±7.78
BMI (Kg/M2)	22.20±3.27
Gender	
Male	87 (53.05%)
Female	77 (46.95%)
Residence	
Urban	102 (62.2%)
Rural	62 (37.8%)
APRI Score	1.8 + 0.6.

Table 1: Sample Description

Out of 164 cases, 102(62.2%) were hypertensive, 98(59.8%) diabetic mellitus, 49(29.9%) smoker, Hyperlipidemia 42(25.6%) and Hypomagnesemia 50 (30.5%) as shown in reported in Table 2. Frequency of liver fibrosis by non-invasive marker in patients with non-alcohol fatty liver disease was 10.98% (18/164). Stratification analysis was performed and observed that rate of liver fibrosis by non-invasive marker in patients with non-alcohol fatty liver disease was not statistically significant among different age groups, gender, residential status, obesity and smokers. It was also not statistically significant with hypertension and diabetic mellitus while rate of liver fibrosis by non-invasive marker in patients with non-alcohol fatty liver disease was significantly high in those cases who had hyperlipidemia or hypomagnesemia.

Variables		Liver Fibrosis Yes	Liver Fibrosis No	Total	p-Value
Hypertension	Yes	10 (9.8%)	92 (90.2%)	102	0.538
	No	9 (12.9%)	54 (87.1%)	62	
Diabetic Mellitus	Yes	11 (11.2%)	87 (88.8%)	98	0.901
	No	7 (10.6%)	59 (89.4%)	66	
Hyperlipidemia	Yes	14 (33.3%)	28 (66.7%)	42	0.0005
	No	4 (3.3%)	18 (96.7%)	122	
Hypomagnesemia	Yes	14 (28%)	36 (72%)	50	0.0005
	No	4 (3.5%)	110 (96.5%)	114	

Table 2: Frequency of Liver Fibrosis by Non-Invasive Marker in Patients with Non-Alcohol Fatty Liver Disease

DISCUSSION

Non-alcoholic fatty liver disease (NAFLD) affects up to 30% of the general population and is the hepatic manifestation of the metabolic syndrome [14]. NAFLD is a spectrum of diseases that encompasses simple steatosis, non-alcoholic steatohepatitis (NASH) and fibrosis, which can lead to cirrhosis, liver failure and hepatocellular carcinoma [15]. However, not all patients progress through the full hepatological spectrum of NAFLD [16, 17]. Determinants of progression include diabetes, diet and ethnicity but the most accurate predictor of liver-related mortality is

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presence of liver fibrosis on biopsy [18-20]. It is neither feasible nor desirable to perform a liver biopsy in every patient with suspected NAFLD because the procedure is invasive, associated with potential complications, cost, sampling error and inter-observer variability. Thus, non-invasive liver tests (NILTs) have been developed as an alternative to liver biopsy. These can be biomarker based or based on routinely collected clinical and laboratory data such as NAFLD fibrosis score (NFS), Fib-4, BARD, aspartate transaminase (AST) to platelet ratio index (APRI) and the AST/alanine transaminase (ALT) ratio [21]. Liver stiffness, measured by transient elastography (TE), acoustic radiation force impulse or MRI can be a surrogate marker of fibrosis, but requires specialist equipment and/or skilled personnel to conduct the tests [22]. In this study the mean age of the patients was 48.15±11.13 years and duration of NAFLD was 10.32±2.93 week while in the study by Kim *et al.*, the mean age was reported to be 44±6.7 years. There were 46.95% male and 53.05% female. Out of 164 cases, 62.2% were hypertensive, 59.8% diabetic mellitus, 29.9% smoker, Hyperlipidemia 25.6% and Hypomagnesemia 30.5%. The prevalence of NAFLD has increased rapidly over the past two decades in the Asia-Pacific region. NAFLD is not uncommon in subjects who are considered non-obese. Previous studies have reported a prevalence of NAFLD that ranges from 7.27% to 23.4% in the non-obese population [23]. In this study frequency of liver fibrosis by non-invasive marker in patients with non-alcohol fatty liver disease was 10.98%. Wai *et al.*, validated the aspartate aminotransferase-to-platelet ratio index (APRI) score in patients with chronic liver disease as value more than 0.6, while our study reported an APRI score of 1.8 [12]. Vernon *et al.*, reported the prevalence for liver fibrosis through APRI in NAFLD is 15% [13]. In a prospective study of 400 US military personnel and their families (mean age 55 years), the prevalence of NAFLD by ultrasound was 46% [24]. Factors associated with NAFLD included male sex, increasing age, and the presence of systemic hypertension, obesity, or diabetes which are in line with the results of our study. In a population-based sample that included 2133 subjects from the US who reported moderate or no alcohol intake, hepatic steatosis was present in 30 and 32%, respectively [25]. Estimates of prevalence of NAFLD in Asia-Pacific regions range from 5 to 30%, depending upon the population studied [26]. In the United States, studies report a prevalence of NAFLD of 10 to 46%, with most biopsy-based studies reporting a prevalence of liver fibrosis from 3 to 5 percent while our study reported twice of that prevalence i.e., 10.98% [25]. Worldwide, NAFLD has a reported prevalence of 6 to 35% (median 20%).

CONCLUSIONS

In this study frequency of liver fibrosis by non-invasive marker in patients with non-alcohol fatty liver disease was 10.98%. APRI is noninvasive and a simple calculation of two laboratory variables and can easily be used at the bedside or in an outpatient setting to assess the liver fibrosis. In this way we can improve the management of NAFLD and to prevent its development, clinicians should be particularly aware of the possibility of NAFLD inpatients.

Conflicts of Interest

The authors declare no conflict of interest.

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