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ULTRASONOGRAPHIC ASSESSMENT OF HEPATIC STEATOSIS AND ITS CORRELATION WITH BMI AND SERUM PARAMETERS OF LIVER FUNCTION IN NON- ALCOHOLIC FATTY LIVER DISEASE

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ABSTRACT

BACKGROUND: *The prevalence of non-alcoholic fatty liver disease (NAFLD) is high in the Western population and is on the rise globally. Similar to alcohol-induced liver damage, pathological alterations in fatty liver can result in end-stage liver disease. Obese or overweight individuals have a higher frequency of non-alcoholic fatty liver disease (NAFLD) than the general population, and it appears that those with a high body mass index (BMI) or abnormalities in certain laboratory tests are more likely to have severe fatty liver and high-grade NAFLD on ultrasonography (U.S.).*

OBJECTIVE: *To evaluate the correlation of BMI and laboratory tests (Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST)), with ultrasonographic grades assessment of hepatic steatosis.*

MATERIALS AND METHODS: *It was a cross-sectional study. Our study was carried out in the Department of Radiology, Pakistan Kidney and Liver Institute, Lahore. A sample size(n) of 35 patients was estimated by the use of the following formulae; Total sample size= N= [(Zα+Zβ)/C]2 + 3= 35 Where, C= 0.5* ln[(1-r)] = 0.5763, Zα= 1.9600, Zβ= 1.2816, (r= 0.562) (19). Non-probability consecutive sampling technique was used. Inclusion criteria as adult patients of both genders over the age of 18, fatty liver on U.S diagnosed if the liver echogenicity is more than that of the renal cortex and spleen and there was attenuation of ultrasound wave, loss of diaphragm contour, and poor outlining of the intrahepatic architecture. After the approval from ethical research committee,*

informed consent was taken from the patients fulfilling the inclusion criteria. Data analysis was done using the statistical package for social sciences (SPSS) version 20. The p-value ≤ 0.05 was considered as significant.

RESULTS: *We discovered that 49.19% of the study group had hepatic steatosis, and 65% of the patients were overweight or obese when they first arrived. Hepatic steatosis was closely associated with a drop in HDL and an increase in AST, and GGT; this incidence was higher in men. The best predictors, according to an ordinal logistic regression model, were BMI and AST.*

CONCLUSION: *According to our findings, the most useful indicators of fatty liver disease severity and ultrasonography grade (USG) in patients with NAFLD are BMI and TG. BMI, however, can be useful as a predictor. However, because AST varies depending on a number of factors, it has not proven a trustworthy result.*

KEYWORDS: *Ultrasonographic Assessment, Hepatic Steatosis, BMI, Serum Parameters, Liver Function, Fatty Liver Disease*

INTRODUCTION

Hepatic steatosis or Non-alcoholic Fatty Liver Disease (NAFLD) is a condition characterized by abnormal accumulation of lipids within the cytoplasm of hepatocytes (1-3). This buildup of fat is not caused by heavy alcohol use. Hepatic Steatosis, which is associated with type 2 diabetes, insulin resistance. Central obesity, and dyslipidemia, results in morbidity and mortality due to the progression to steatohepatitis, fibrosis, and cirrhosis (4-5).

The prevalence of fatty liver in Pakistani general population is l5% (6). Nonalcoholic fatty liver disease ranges from nonalcoholic fatty liver (NAFL) to nonalcoholic steatohepatitis (NASH) based on histologic analysis. Though NAFL and early-stage NASH may be reversible, hepatic cirrhosis is irreversible and may progress to decompensated liver cirrhosis (7). In fact, NASH is expected to become the most common etiology for liver transplantation in the next l0to20 years (8-9). ln addition, prevalence among obese people is far higher than general population (10), Some studies have proposed that obese or overweight people have more advanced NAFLD (11).

Diagnostic methods for NAFLD are imaging, liver biopsy, laboratory tests including Alanine aminotransferase (ALT) and aspartate aminotransferase (AST), Hepatitis B or C serology and workup for autoimmune and Wilson's disease (12). Among imaging methods, Magnetic Resonance imaging (MRI) is the gold standard for diagnosis of fatty liver, but the usage of MRI is limited because it is expensive and not easily available (13).

CT scan is more widely available; however, it comes with the risks ofradiation exposure. Ultrasound (U.S) is a cheap, readily available, safe and non-invasive method which provides appropriate information about hepatic steatosis (H.S) (14). Its sensitivity and specificity in detecting moderate to severe fatty liver are comparable to those of histology (15). Commonly, NAFLD is diagnosed by U.S and categorized into Grades I, II and Ill. High grade of NAFLD in U.S is related to the end stage of liver disease (16). However, U.S is not sensitive towards detection of liver inflammation, so biopsy of liver is required to confirm the diagnosis.

Previous studies have shown that fatty liver disease was closely related to deranged serum parameters of the liver function (ALT and AST)(17). Few others showed that majority of patients with NAFLD were obese (18). Some stated that patients with fatty liver disease had a significant higher body mass index (BMI),(r= 0.52, P= 0.001) (19).

NAFLD can be diagnosed using a variety of techniques, such as liver biopsy or laboratory testing along with imaging techniques (20). Magnetic Resonance Imaging (MRI) is the gold standard among imaging techniques for diagnosing fatty liver, but its use is restricted due to its high cost (21). We can also employ ultrasonography (U.S.) and computed tomography (CT) scans (22). Overall, the U.S. is more sensitive than a CT scan to identify fatty alterations in the liver, with the exception of some localized and patchy hepatic changes (22). A helpful, secure, and non-invasive technique that offers pertinent information on hepatic steatosis (H.S.) is U.S. (23).

Only in the United States is NAFLD classified into three stages: mild, moderate, and severe. 10% to 30% of hepatocytes are engaged in the mild stage, 30% to 70% in the moderate stage, and over 70% in the severe stage (18). The end stage of liver disease is associated with high grade NAFLD in the United States (21, 22). Obesity and Body Mass Index (BMI), diabetes, hyperlipidemia, age, and metabolic syndrome (MS) are some characteristics that appear to be effective in the process and progression of NAFLD and ultrasonography grade (USG) (23–24). The impact of lipid profiles or liver enzymes, however, is up for debate.Some papers supported the idea that liver enzymes have an impact on U.S. grades, while others suggested that the disease process and U.S. grades could be influenced only by lipid profiles or specific liver enzymes (25).

These studies, however, did not mention the correlation of sonographic grading of fatty liver with deranged serum parameters of liver function (ALT and AST) and raised BMI. Hence, this study was attempted to evaluate the correlation of different sonographic grades of fatty liver with BMI, and serum parameters of liver function (ALT and AST) in patients of fatty liver disease.

MATERIALS AND METHODS

It was a cross-sectional study. Our study was carried out in the Department of Radiology, Pakistan Kidney and Liver Institute, Lahore. Duration of the study was 3 months after the approval of the synopsis. A sample size(n) of 35 patients was estimated by the use of the following formulae; Total sample size= $N= [(Z\alpha+Z\beta)/C]2 + 3= 35$ Where, $C= 0.5* \ln[(1-r)] = 0.5763$, $Z\alpha= 1.9600$, $Z\beta= 1.2816$, ($r= 0.562$) (19). Non-probability consecutive sampling technique was used. Sample was collected with the inclusion criteria as adult patients of both gender over the age of 18, fatty liver on U.S diagnosed if the liver echogenicity is more than that of the renal cortex and spleen and there was attenuation of ultrasound wave, loss of diaphragm contour, and poor outlining of the intrahepatic architecture. While, the exclusion criteria were alcoholic patients, subjects diagnosed as Hepatitis B and C, known cases of chronic liver disease and cirrhosis, patients with systematic comorbidities and neoplasm, and patients who used hepatotoxic drugs during past 6 months. After the approval from ethical research committee, informed consent was taken from the patients fulfilling the inclusion criteria. A questionnaire/Proforma was constructed to collect patient's biodata, BMI and serum parameters values. To measure height, the measurement scale was fixed to the wall. Height without shoes was measured when the subject was standing with heels, buttocks, shoulders and occiput touching the vertical scale. Patients weight was measured by the weighing scale. BMI was calculated using height and weight of the patient. Assessment of Liver on Ultrasound using Ultrasound Machines GE LOGIQ P7 and GE LOGIQ S8 with curvilinear probe 3.5-6.5MHz. To remove bias, abdominal U.S. was performed by a radiologist blinded to any relevant clinical information (BMI or values of serum parameters).All this information was recorded in the pre-designed Proforma (attached).

Data analysis was done using the statistical package for social sciences (SPSS) version 20. Pearson correlation was used to find a relationship between sonographic liver echogenicity with BMI and serum liver function tests. Quantitative variables like age and BMI were presented as mean ± SD. Qualitative variables like gender, grades of hepatic steatosis were presented as frequency and percentage. Data was strategized for age and gender. Pearson correlation was calculated post-stratification. The p-value ≤ 0.05 was considered as significant.

RESULTS

A total of 35 cases, 20 of which were male (65.7%) and 15 of which were female (34.3%), ranging in age from 18 to 60, were examined. In total, 15 patients (44.1%) were overweight, and 9 cases (28.0%) were obese. The majority of the patients in our study were in grade 2 in the United States and ranged in age from 35 to 44. Age, BMI, were all associated with USG, according to a comparison of data using Pearson's Chi-Square test in various USG; BMI (p-value ≤ 0.001) were statistically significant to USG. Age, AST, ALT, levels did not show any significant values. Table 1 describes the most significant clinical features of NAFLD patients.

Table 1 : Demographical, Clinical Data According to Analysis of Patients With NAFLD.

Age	Percentage	Min	Max	P-Value
1	32	18	60	0.034
2	54	18	60	
3	14	18	60	
Total	35	18	60	
BMI				<0.001
1	38	22	40	
2	46	16	32	
3	14	23	33	
Total	100	18	37	
AST				0.134
1	30	19	192	
2	54	15	287	
3	18	13	189	
Total	100	15	293	
ALT				0.453
1	49	14	522	
2	42	15	529	
3	15	24	212	
Total	100	13	514	

Comparisons of the mean liver function tests, including ALT and AST levels, in various USG. When comparing the moderate and severe groups, there was statistically significant difference in mean ALT and AST levels (P = 0.041, 0.021, respectively). Each variable's relationship to USG was plotted. More association may be shown in the gradient of increases regarding age and BMI between grades 2 and 3. BMI and AST were the most associated indicators to predict the severity of fatty liver based on the patient's ultrasonography grade, according to the results of ordinal logistic regression, which was used to identify the most efficient predictors on USG.

Table 2 : Odds Ratio (OR) for Independent Variables Associated to Ultrasonography Grades "Mild" and "Moderate" to "Severe".

Variables	OR	95% CI	P value
Gender	1.38	0.62-2.78	0.028
AST	1.42	0.80-2.60	0.011
ALT	1.20	0.60-2.20	0.029

DISCUSSION

The study's main conclusions center on the effectiveness of hepatic ultrasonography (U.S.) in identifying and measuring hepatic steatosis in patients with nonalcoholic fatty liver disease (NAFLD). The study's findings comprising one of the biggest cohorts with biopsy-proven NAFLD ever documented showed a strong correlation between the ultrasonographic steatosis score (USS) and the degree of steatosis seen after a liver biopsy. According to these findings, an ultrasound examination is a good way to screen for non-alcoholic fatty liver disease (NAFLD) and a practical non-invasive way to measure hepatic steatosis. Furthermore, serum ALT and AST are not useful in determining if additional work-up is necessary in obese persons with suspected fatty liver disease since we observed that serum aminotransferases had low predictive value regarding the existence or severity of fatty liver disease.

The most common radiographic modality for evaluating fatty liver is U.S., which has long been acknowledged as a helpful screening tool for NAFLD (3). The majority of the data that is currently available on the use of U.S. to diagnose steatosis has been in adult populations and is retrospective in nature (5-7). In a

recent study, Chiloiro et al. (4) examined the correlation between the metabolic profile, adipose tissue distribution, and ultrasonographic diagnosis of fatty liver in 94 patients who were moderately obese but did not have access to liver biopsy. While there was no statistically significant correlation between fatty liver on U.S. and elevated blood ALT and AST levels, fatty liver on U.S. was favorably correlated with anthropometric parameters, insulin resistance, and other metabolic abnormalities linked to obesity.

Our current investigation confirms the lack of link between serum transaminases and both liver biopsy and U.S. determinations of fatty liver, and it also shows a high positive correlation between USS and the degree of steatosis on liver biopsy. Since blood transaminase levels are the only criteria used by current screening guidelines to identify and conduct additional workup on patients at risk of NAFLD, these findings are extremely significant. According to our present data and the expanding body of research addressing the shortcomings of blood liver enzymes in the assessment of non-alcoholic fatty liver disease (NAFLD), hepatic U.S. is a more reliable option for screening who are at risk.

Similar to earlier findings in adult population studies, we discovered that hepatic U.S. was unable to distinguish between NAFLD and NASH (5,7). According to a prospective adult study examining the use of U.S. in identifying hepatic steatosis, there was no significant correlation between U.S. findings and either the grade of inflammation or the degree of fibrosis, and none of the U.S. findings could differentiate between steatosis and NASH. Moreover, ≥20% was the lowest level of steatosis that could be identified by U.S. and had the strongest association with histological results (5).

Our research strengthens the conclusion that moderate to severe steatosis improves U.S. sensitivity and specificity in measuring steatosis. In our investigation, a USS of 2 exhibited a nearly 80% sensitivity in identifying moderate to severe steatosis. Determining USS, among patients was not helpful for quantifying inflammatory activity and stage of fibrosis, and it was unable to differentiate between steatosis and NASH, as has been documented in the adult population. These findings reinforce the necessity of creating new, trustworthy biomarkers for risk assessment and tracking how well patients with NAFLD respond to treatment.

The inclusion of a sizable sample of consecutively recruited adolescents with liver biopsy-proven NAFLD exhibiting the entire spectrum of illness in whom U.S. was conducted within a month of the liver biopsy procedure is one of our study's key features. One of the study's limitations is that the patients were examined at a big referral tertiary care medical center, which means that the findings might not apply to children with NAFLD in the community. Second, it was impossible to assess intra- and inter-observer variability because US tests were only reviewed once by a single radiologist.

Finally, because only a small percentage of patients in the current study had a USS of zero, we were unable to assess possible reasons why the U.S. failed to detect steatosis. It is necessary to conduct more research to assess U.S. as a longitudinal follow-up technique. With a good correlation between USS and the grade of steatosis on liver biopsy, our findings suggest that hepatic U.S. is a valuable tool for measuring steatosis in patients with suspected NAFLD. Since normal liver enzymes are not good indicators of fatty liver disease, an ultrasound examination of the liver should be the first screening method.

CONCLUSION

According to our findings, the most useful indicators of fatty liver disease severity and ultrasonography grade (USG) in patients with NAFLD are BMI and TG. BMI, however, can be useful as a predictor. However, because AST varies depending on a number of factors, it has not proven a trustworthy result.

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