ORIGINAL ARTICLE

CORRELATION BETWEEN SERUM LIVER ENZYMES AND FIBROSIS SEVERITY IN NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) PATIENTS. A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: One of the major chronic liver diseases in the world is NAFLD which tends to start as mere steatosis but tends to evolve into fibrosis and cirrhosis. Serum liver enzymes are common measurement of hepatocellular damage which is however not predictable regarding its association with the severity of fibrosis. This was done to determine the connection between serum liver enzyme levels and the severity of fibrosis in NAFLD patients by non-invasive means of assessment.

Methods: The present study is a cross-sectional one that was carried out at a tertiary care hospital located in Punjab, Pakistan, between January 2023 and March 2024, including 100 patients with a diagnosis of NAFLD according to ultrasound results. Patients who consume alcohol, those with viral hepatitis and other liver-related pathologies were excluded. The normal range of serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT) were also conducted by standard enzymatic methods. Transient elastography was used to quantify the level of fibrosis and the stages of fibrosis F0–F4 were measured. Pearson correlation and ANOVA tests were applied in order to analyze statistical correlations.

Results: Out of 100 patients (58 men, 42 women; median age, 47.6 + 9.8 years) serum liver enzymes became elevated directly in proportion to fibrosis stage. AST and ALT mean levels were very different in the case of advanced fibrosis (F364) and mild fibrosis (F0-F1). Fibrosis stage and AST (r = 0.71), ALT (r = 0.68), GGT (r = 0.63), and ALP (r = 0.57) were statistically significantly positively correlated to a strong degree.

Conclusion: Liver enzymes in serum especially AST and ALT exhibit significant correlation with severity of fibrosis in NAFLD patients. These are easily accessible biomarkers which can be considered useful non-invasive biomarkers of identifying those patients who are at risk of advanced fibrosis which would be crucial in early interventions and enhanced disease monitoring.

Keywords: Non-Alcoholic Fatty Liver Disease, Liver Enzymes, Fibrosis, AST, ALT, Transient Elastography, GGT, ALP

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INTRODUCTION

Non-Alcoholic Fatty liver Disease (NAFLD) is an eminent health concern of interest in the globe, the continuum of liver diseases, which involve simple steatosis to non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and hepatocellular carcinoma[1]. It is a disorder that is characterized by excess accumulation of hepatic fat in individuals who have limited or no alcoholic intake. Due to the increased incidence of obesity, diabetes mellitus, dyslipidemia and metabolic syndrome, NAFLD has now

become the number one cause of chronic liver disease in the world and is currently prevalent in roughly 25% of the world population[2].

The pathogenesis of NAFLD is multifactorial and it comprises resistance to insulin, oxidative stress, lipid peroxidation, dysfunction of the mitochondrion, and release of inflammatory cytokines[3]. All of these processes combined contribute to the work of hepatocellular damage, fibrosis, and the progression of the disease. Identifying patients at risk of progressing to the advanced fibrosis stage is also necessary because the amount of fibrosis is the best prognosticator of the final outcomes, including liver-related mortality and cardiovascular-related problems[4].

Serum liver enzymes are the most regularly used biomarkers in the evaluation of hepatic injury and comprise alanine aminotransferase (ALT) aspartate aminotransferase (AST), alkaline phosphatase (ALP) as well as gamma-glutamyl transferase (GGT). Although high liver enzyme is a well-known indicator of hepatocellular injury, their connection to histologically validated degrees of fibrosis in NAFLD have nevertheless not been brought to fruition[5]. It will have instances of patients with high level of fibrosis but normal level of enzymes as well as patient with low levels of fibrosis but with a significantly high level of enzyme. Therefore, one should be aware of the relationship between those biochemical markers and a stage of fibrosis that allow determining those patients who require the further diagnostic test or the follow-up treatment[6].

Such non-invasive techniques as serum biomarkers and fibrosis are gaining momentum in clinical practice due to the high limitations and risks of using liver biopsy, which is the gold standard of assessing hepatic fibrosis[7]. The relationship between ordinary liver enzyme values and the degree of fibrosis can be investigated to maximize the diagnostic worth of laboratory parameters that are inexpensive and can be easily measured in patients to the categorization of NAFLD patients according to the intensity of disease severity[8].

The study will be aimed at determining the correlation amidst serum liver enzymes and the magnitude of fibrosis in NAFLD patients. Having such associations considered, the study will strive to make a contribution on enhancing non-invasive-based diagnostic approaches, early diagnosis and improved clinical care of individuals who are at risk of accelerated liver injury[9].

MATERIALS AND METHODS

This study was a cross-sectional study and conducted at the Department of Gastroenterology and Hepatology of a tertiary care hospital situated in Punjab, Pakistan, during the period between January 2023 and March 2024. A sample of 100 and ten patients with Non-Alcoholic Fatty Liver Disease (NAFLD) was recruited by non-probability consecutive sampling. The NAFLD diagnosis has been based on the ultrasonographic-hepatic steatosis without excessive alcohol use (Less than 20g/day of females and 30g/day of males), hepatitis with viruses (HBsAg and anti-HCV negative), or other forms of secondary hepatitis. The report disqualified patients with chronic alcohol consumption, viral hepatitis, autoimmune liver disease, hemochromatosis, Wilson disease and patients on hepatotoxic medications.

With informed consent, all the demographic information including age, gender, body mass index (BMI), medical history, and clinical results were provided in a structured proforma. The biochemical testing was conducted using the Venous blood samples one collected following an overnight fast. The level of serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT) were determined using standard enzyme-linked procedures of colorimetric on an automated chemistry analyzer. The other parameters were measured in terms of fasting blood glucose, lipid profile and body mass index to establish the metabolic risk factors of the same.

The extent of hepatic fibrosis was determined in regards to transient elastography which was capable of measuring the liver stiffness of the liver in kilopascals (kPa) on a non-invasive scale. According to the standard cut off values, patients were categorized as fibrosis (F0-F4) and F0-F1 mild fibrosis, F2 moderate, F3 advanced and F4 cirrhosis. The correlation of serum liver enzyme with the levels of fibrosis was established to test the possibility that these biomarkers readily available on a regular basis reflect the levels of liver fibrosis in NAFLD.

Whole laboratory work was done under stringent quality control procedures as per the institutional biosafety policy. Statistical package of the social sciences (SPSS) version 26.0 was used in analyzing and inputting the data. Continuous variables were expressed in terms of mean +SD whereas the nominal variables were expressed in terms of frequencies and percentages. The correlation of the degree of liver enzyme and the extent of fibrosis had to be assessed with the help of Pearson correlation coefficient and ANOVA tests. The p-value was considered to be statistically significant (lower value than 0.05).

RESULTS

This study involved 100 patients with Non-Alcoholic Fatty Liver Disease (NAFLD), male and female patients were equal in number (58 and 42 respectively). The participants consisted of 47.6 (SD = 9.8) years, with body mass index (BMI) of 30.8 (SD = 4.5) kg/m 2, which reflects that most subjects are overweight and obese. Table 1 shows the demographic and baseline clinical data of NAFLD patients. Most of the patients were obese and middle-aged which represented the metabolic risk group mostly prevalent in NAFLD. The presence of high levels of fasting glucose and lipids means that there is a high

likelihood of co-occurrence of metabolism syndrome elements in this cohort.

Table 1: Demographic and Clinical Characteristics of Study Participants

Variable	Mean ± SD / n (%)
Total Patients	100
Age (years)	47.6 ± 9.8
Gender (Male/Female)	58 (58%) / 42 (42%)
BMI (kg/m²)	30.8 ± 4.5
Fasting Blood Glucose (mg/dL)	122.4 ± 22.6
Total Cholesterol (mg/dL)	212.5 ± 37.4
Triglycerides (mg/dL)	186.3 ± 45.7

Table 2 shows a gradual rise in serum liver enzymes levels as the fibrosis severity is progressed. There was a significant increase in the values of ALT and AST in patients who had F3 and F4 stages versus patients having mild fibrosis (F 0-F1). On the same note, ALP and GGT level showed a gradual rise implying that there was a close biochemical relationship between the level of enzymes and the fibrosis stage of the histology.

The results of Table 3 provide substantial positive relationships between the level of serum liver enzymes and the degree of fibrosis. AST (r = 0.71), ALT (r = 0.68) and GGT (r = 0.63), and ALP (r = 0.57) showed the highest correlation. Such results suggest that an increase in transaminases and cholestatic enzyme levels is strongly linked with the development of hepatic fibrosis in NAFLD patients.

Table 2: Serum Liver Enzyme Levels Across Different Fibrosis Stages (F0–F4)

Fibrosis Stage	n (%)	ALT (U/L) Mean ± SD	AST (U/L) Mean ± SD	ALP (U/L) Mean ± SD	GGT (U/L) Mean ± SD
F0–F1 (Mild)	32 (32%)	46.8 ± 11.3	39.6 ± 9.8	82.5 ± 18.6	65.2 ± 14.5
F2 (Moderate)	28 (28%)	58.4 ± 13.1	48.3 ± 11.7	91.8 ± 21.4	79.1 ± 17.3
F3 (Advanced)	24 (24%)	71.5 ± 14.8	59.6 ± 12.5	104.3 ± 26.2	93.4 ± 21.6
F4 (Cirrhosis)	16 (16%)	85.7 ± 15.4	74.2 ± 13.9	121.5 ± 30.8	108.7 ± 25.1

Table 3: Correlation Between Liver Enzymes and Fibrosis Severity

Parameter	Correlation Coefficient (r)	p-value
ALT vs Fibrosis Stage	0.68	<0.001
AST vs Fibrosis Stage	0.71	<0.001
ALP vs Fibrosis Stage	0.57	0.002
GGT vs Fibrosis Stage	0.63	<0.001

The results of this article illustrate that the high levels of liver enzymes, in particular, AST and ALT, in the serum are capable predictors of the degree of hepatic fibrosis in NAFLD patients. These elevation lines of enzymes have not been applied as exclusive in fibrosis, but the specified linear quality of the lines at the advancing stages of fibrosis lead to the purpose of enzyme levels as accessible biochemical indicators to develop the disease. The statistical analysis revealed that the functional tests of liver human organ are found to be significantly high (p -values less than 0.05) and are applicable to clinical cases of non-invasive fibrosis.

DISCUSSION

The current paper has discussed the correlation between serum liver enzymes and hepatic necrosis of the liver regarding the patient with Non-Alcoholic Fatty Liver Disease (NAFLD). It was discussed that the high levels of liver enzymes mainly AST, ALT, ALP, and GGT had a significant and statistically significant correlation with progressive degrees of fibrosis using transient elastography[10]. The most significant correlation was proved to be level in AST whereby, it is more diagnostic to identify the evidence of liver damage in the advanced stage[11].

Such outcomes are consistent with the clinical observation that as NAFLD steatosis advances into steatohepatitis and fibrosis, hepatocellular damage is observed to cause an enzyme leakage into the blood. Cytoplasmic and mitochondrial injury are markers of hepatocellular injury, and they are ALT and AST, respectively[12]. These results suggest that there is an inclination to an increment in the enzyme levels as the fibrosis increases suggesting that the prolongation of inflammation and necrosis result in structural modifications of the liver. In addition, an increase in AST/ALT ratio in late disease can be used to confirm that as the extent of fibrosis is massive, the mitochondrial injury is the first[13].

The other similar increase of ALP and GGT noted in the stages of fibrotic was also noticed in the study that could be blamed on the cholestatic stress, proliferation and oxidative stress usually associated with progressive NAFLD. This tendency can be considered the sign of the fact that NAFLD liver injury is multifactorial due to the significant role of both hepatocellular and biliary pathways[14,15].

These results are suggestive of the potential usefulness of the routine liver function tests as non-invasive indices of the measure of the amount of the fibrosis. As liver biopsy is intrusive, costly and prone to sampling error at the time a cheaper and safer option of diagnostics may be found in the application of biochemical parameters and elastography[16]. However, it is also important to note that the normal ranges of liver enzymes

are not always sufficient in excluding the progressive fibrosis. This bullet point may be mistaken into thinking that the normal ALT and AST level may be seen in certain patients in spite of the massive histological loss, be it due to the reduction in the mass of the hepatocyte or due to the variability of the enzyme activity[17].

The NAFLD population in this demographic, in turn, is also supported by the demographic characteristics of this investigation since, first of all, they are not young and active, and their dyslipidemia, damaged glucose, and so-called obese individuals form the general population[18]. These metabolic impairments facilitate insulin resistance, lipid deposition and oxidative stress, the fundamentals of fibrosis. Labour markers make it possible to identify the risk patients early to implement necessary interventions on a timely basis through lifestyle change, weight management, and pharmacological intervention[19].

Although the results are rational and relevant clinically, there must be certain weaknesses. This study is cross-sectional; thus, making it impossible to establish a causal relationship between the enzyme lift up and the growth of fibrosis[17]. The diagnostic accuracies have some limitations as the test does not have absolute histopathological confirmation that can be performed on liver biopsy thus it has slight limitations on diagnostic accuracy. Moreover, 100 patients are also enough to reveal the preliminary analysis, but not the whole clinical image of NAFLD in a general population[20].

On the whole, the current research has revealed the existence of the identified biochemical correlation between the serum levels of liver enzymes and the extent of fibrosis in NAFLD patients. The AST and ALT values that are high and have been supported by higher values of GGT and ALP can be considered cheap measures of hepatic fibrosis. The outcomes would be useful in informing the clinical significance of the integration of a combination of regular liver enzymes tests and non-invasive imaging methods to diagnose and monitor NAFLD in order to stratify risks in NAFLD management[11-19].

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