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ASSOCIATION OF LIVER ENZYME ALTERATIONS AND GLYCEMIC STATUS IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE: A CROSS-SECTIONAL STUDY AT A TERTIARY HEALTHCARE INSTITUTE

Biochemistry

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ABSTRACT

Background Non-alcoholic fatty liver disease (NAFLD) is one of the most common chronic liver diseases worldwide and is closely associated with metabolic abnormalities such as obesity, dyslipidemia, and diabetes mellitus. Despite its increasing prevalence, NAFLD often remains underdiagnosed because many affected individuals present with normal liver enzyme levels. **Objective** To evaluate the association between liver enzyme alterations and glycemic status among patients with non-alcoholic fatty liver disease attending a tertiary healthcare institute. **Methods** A cross-sectional observational study was conducted over a period of twelve months among 400 adult participants attending the outpatient department of a tertiary care hospital. Individuals aged ≥18 years without a history of alcohol consumption were included. Patients with known liver disease, chronic illness, or those on medications affecting liver enzymes were excluded. Sociodemographic and clinical information was collected, and biochemical investigations including liver enzymes (AST, ALT, ALP, GGT), fasting blood glucose, and lipid profile were performed. Associations between NAFLD and metabolic variables were analyzed using the chi-square test. **Results** The overall prevalence of NAFLD in the study population was 18.8%. NAFLD was most frequently observed among individuals aged 36–60 years. Although females constituted a slightly higher proportion of the study population, NAFLD prevalence was higher among males (20%) compared to females (17.1%). A significant association was observed between NAFLD and higher body mass index, diabetes mellitus, hypertension, dyslipidemia, and impaired fasting glucose levels ($p < 0.05$). Mild elevations of liver enzymes were observed in a small proportion of participants; however, more than 90% of NAFLD patients had normal liver enzyme levels, and no statistically significant association was observed between liver enzyme elevation and NAFLD. **Conclusion** NAFLD shows a strong association with metabolic risk factors including obesity, diabetes mellitus, hypertension, and dyslipidemia. Since many individuals with NAFLD may present with normal liver enzyme levels, screening of high-risk individuals with metabolic abnormalities is essential for early detection and prevention of disease progression.

KEYWORDS

Non-alcoholic fatty liver disease; Liver enzymes; Glycemic status; Diabetes mellitus; Metabolic syndrome

INTRODUCTION:

NAFLD is defined by excessive fat accumulation in hepatocytes (>5% of liver weight) in individuals who consume little or no alcohol and in the absence of other causes of hepatic steatosis [1]. NAFLD related burden is under-assessed due to lack of awareness among the people, long natural history for the development of fibrosis and mortality not directly related to liver. Moreover, its chronicity involves other metabolic changes like altered liver functions, impaired glucose metabolism, and insulin resistance which increases morbidity in the affected individuals. These metabolic disturbances contribute not only to the initiation of hepatic steatosis but also to disease progression and extrahepatic complications, particularly cardiovascular disease, which remains the leading cause of mortality in NAFLD patients [2].

The second largest organ- liver helps in various functions like secretory, metabolic, hematologic, detoxification, immunologic and storage function [2]. The liver function parameters can note the extent of liver damage. The abnormal levels of liver enzymes can indicate damage to the liver or changes in bile flow. The histopathological changes of NAFLD includes- Steatosis, Steatohepatitis, Fibrosis & Cirrhosis. The biochemical picture of NAFLD consists of slightly increased activity of amino transferase enzymes (not more than 4 times the upper reference value). In NAFLD, GGT concentrations can be increased up to 3 times the upper reference limit in 50% of patients with NAFLD lacking alcohol consumption [3]. Elevated GGT level is associated with increased severity of NAFLD that adds increased mortality. ALP levels may get elevated in non-alcoholic steatohepatitis which may increase up to 2-3 times the upper reference range. On the contrary, about 78% of patients with NAFLD may have normal liver enzymes.

Diabetes mellitus is a major non communicable accounting for about 90% of all the cases that is more prevalent in men and it consists of a group of metabolic diseases characterized by hyperglycemia which is caused by insulin secretion defects, insulin's action or both [4]. The worldwide prevalence of diabetes mellitus was 2.8% in 2000 and is estimated to rise to 4.4% in 2030. The incidence of NAFLD in individuals with T2DM is estimated at around 70% to 75%. India is now the world's diabetic capital and NAFLD has emerged as a major cause of liver disease among its population. Several studies show that T2DM patients with NAFLD are highly prone to progressive forms of NAFLD like NASH, liver fibrosis, hepatocellular carcinoma development and liver related mortality. While, NAFLD patients have a high prevalence of prediabetes and the presence of NAFLD predicts the T2DM development [5]. Consequently, evaluation of liver enzymes and glycemic status is fundamental for understanding disease pathophysiology, assessing severity, and guiding management strategies.

Aim:

To study the changes of liver enzymes, and glycemic status among the patients of Non -alcoholic Fatty Liver Disease (NAFLD).

Materials & Method:

A cross- sectional observational study was conducted over a period of 12-months at a tertiary care hospital. Using convenient sampling 400 participants were incorporated in the study from the Out Patient Department. The study participants included both males and females of age ≥ 18 years, attending the outpatient department (OPD) with general complaints and without the history of alcoholism. Persons with history of alcoholism, hepatic illness, chronic illness, critical illness, on drugs which alter liver enzymes levels and pregnant individuals were excluded. The study was approved by the Institutional ethical committee and conforms to the Helsinki declaration. Informed consent was obtained from the participants. A detailed socio-demographic details were taken & then the subjects were evaluated for the liver enzyme and glycemic status.

RESULTS & DISCUSSION:

In our study 400 participants belonged to urban population with slightly female predominant proportion and < 60 years of age i.e. NAFLD was more prevalent among the age group 36-60 years followed by >60 years. The overall prevalence of NAFLD observed in the study was 18.8%, which is comparable with several hospital-based studies conducted in India (table no.1). However, population-based studies have reported higher prevalence rates, which may be attributed to differences in lifestyle factors, dietary patterns, and study methodologies. Majumdar A et al had conducted a population- based study on rural population of Haryana and found a prevalence of 30.7% [6]. A similar population-based study conducted in India by

Amarakpur D et.al showed a higher prevalence of NAFLD among 40 – 60 years of age [7].

Among the NAFLD subjects, males (20%) were affected more frequently than females (17.1%) (Table no. 1). Similar findings of male preponderance had been observed in various studies like a large Dutch cohort study by van den Berg E.H et.al, [8] & a multicenter large retrospective study conducted in Japan by Eguchi Y et.al. [9]. On the contrary a population- based cross-sectional study conducted in Thailand by Summart U documented a female preponderance in all age groups, but large difference was observed between 56-60 yrs [10].

Table no.1: Socio-demographic profile of the study population:

Variables		No. of Subjects	Percentage (n%)
Age	18 – 35 yrs	110	27.5
	36- 60 yrs	236	59
	> 60 yrs	54	13.5
Sex	Male	188	47
	Female	212	53
BMI	18.5 – 22.5 kg/m^2	88	22
	23 – 24.9 kg/m^2	74	18.5
	>25 kg/m^2	238	59.5
DM	Yes	100	25
	No	300	75
HTN	Yes	80	20
	No	320	80

A significant association between NAFLD and diabetes mellitus was also observed. The prevalence of NAFLD among diabetic individuals was considerably higher compared to non-diabetic participants. This finding highlights the crucial role of insulin resistance in the pathogenesis of NAFLD (table no.1).

Hypertension and dyslipidemia were also significantly associated with NAFLD in this study. Elevated levels of total cholesterol, triglycerides, LDL-C, and VLDL-C were more frequently observed among individuals with NAFLD. These findings support the concept that NAFLD is closely linked to metabolic syndrome (table no.1).

With respect to liver enzymes, most individuals with NAFLD in the present study had normal enzyme levels. This observation is consistent with previous studies reporting that a substantial proportion of NAFLD patients may have normal liver enzyme values. Therefore, relying solely on liver enzyme levels may lead to underdiagnosis of NAFLD.

Table no. 2: Relationship between Liver enzymes and NAFLD:

Liver Enzymes		No.of subjects	NAFLD	Non NAFLD	Chi-Square test (P-value)
AST	Normal	388	72(18.6)	316(81.4)	0.573
	High	12	3(25)	9(75)	
ALT	Normal	387	70(18.1)	317(81.9)	0.064
	High	13	5(38.5)	8(61.5)	
ALP	Normal	385	72(18.7)	313(81.3)	0.557
	High	15	3(20)	12(80)	
GGT	Normal	371	67(18.1)	304(81.9)	0.154
	High	29	8(27.6)	21(72.4)	

In the present study, one fourth of the study population with an elevated aspartate aminotransferase (AST) had NAFLD while the prevalence among those without AST elevation was found to be lower. Similarly, the prevalence of NAFLD among people with elevated alanine aminotransferase (ALT) levels was higher compared to those without an elevation in AST level. But the association was not statistically significant. In the NHANES III study conducted among US population, 6% of patients with elevated ALT had 41% prevalence of NAFLD and 5.6 % of elevated AST with 33.8% prevalence of NAFLD [11]. ALT elevation was more common among NAFLD patients than AST elevation (table no.2).

NAFLD was present in one fifth of the individuals with elevated alkaline phosphatase (ALP) levels and in roughly one fourth of those with elevated gamma-glutamyl transferase (GGT) levels. But there was no significant association (Table no. 2). A cross-sectional study conducted by Sanyal et.al in eastern India documented a significant association between elevated GGT values and NAFLD and no association between ALP and NAFLD [12]. This could be due to differences in the methods used. More than 90 % of NAFLD patients had normal levels of liver enzymes in the present study. This finding was similar to a study conducted by Browning et.al in among urban population in US with 78% of patients with normal liver enzymes [13].

In our study the prevalence of NAFLD among the diabetic population was almost twice than that of the non-diabetic population and the association is statistically significant. Among NAFLD patients 41.3% had diabetes. A hospital based cross sectional study conducted by Mathew T et.al in Karnataka documented a 52.7% prevalence of NAFLD among pre-diabetes and 30.7% among diabetes [14]. Impaired glycemic status is an established risk factor for the development of NAFLD and our findings are also in agreement with it.

Table no. 3 : Association between Liver enzymes, Glycemic status and NAFLD:

Variables		NAFLD status		χ^2 (df)	P-Value
		Yes (n%)	No (n%)		
Age	18 – 35 yrs	9 (8.2)	101(91.8)	11.372(2)	0.003
	36 – 60 yrs	55(23.3)	181(76.7)		
	>60 yrs	11(20.4)	43(79.6)		
Sex	Male	39(20.7)	149(79.3)	0.926(1)	0.336
	Female	36(17)	176(83)		
BMI	< 18.5 kg/m^2	5(5.7)	83(94.3)	25.719(2)	0.000
	18.5 – 25 kg /m^2	6(8.1)	68(91.9)		
	>25 kg/ m^2	64(26.9)	174(73.1)		
DM	Yes	31(31)	69(69)	13.134(1)	0.000
	No	44(14.7)	256(85.3)		
HTN	Yes	27(33.8)	53(66.2)	14.769(1)	0.000
	No	48(15)	272(85)		
AST	Normal	72(18.6)	316(81.4)	0.317(1)	0.573
	High	3(25)	9(75)		
ALT	Normal	70(18.1)	317(81.9)	3.427(1)	0.064
	High	5(38.5)	8(61.5)		
ALP	Normal	72(18.7)	313(81.3)	0.016(1)	0.899
	High	3(20)	12(80)		
GGT	Normal	67(18.1)	304(81.9)	1.602(1)	0.206
	High	8(27.6)	21(72.4)		
Fasting Glucose	Normal	29(12.7)	200(87.3)	13.197(2)	0.001
	Impaired	25(28.1)	64(71.9)		
	Diabetic	21(25.6)	61(74.4)		

The association between liver enzyme levels and NAFLD was assessed using the chi-square test. In the present study, NAFLD was observed in 18.6% of individuals with normal AST levels and 25% of those with elevated AST levels; however, this association was not statistically significant ($\chi^2(1) = 0.317$, $p = 0.573$). Similarly, 18.1% of individuals with normal ALT levels and 38.5% of those with elevated ALT levels had NAFLD, but the association did not reach statistical significance ($\chi^2(1) = 3.427$, $p = 0.064$). With regard to alkaline phosphatase (ALP), NAFLD was present in 18.7% of individuals with normal ALP levels and 20% of those with elevated ALP levels, with no significant association observed ($\chi^2(1) = 0.016$, $p = 0.899$). Likewise, NAFLD was detected in 18.1% of participants with normal GGT levels and 27.6% of those with elevated GGT levels, though the association was not statistically significant ($\chi^2(1) = 1.602$, $p = 0.206$) (table no.3).

In contrast, a statistically significant association was observed between fasting glucose levels and NAFLD ($\chi^2(2) = 13.197$, $p = 0.001$). The prevalence of NAFLD increased with worsening glycemic status, being 12.7% among individuals with normal fasting glucose, 28.1% among those with impaired fasting glucose, and 25.6% among diabetic individuals (table no.3).

CONCLUSION:

Non-alcoholic fatty liver disease is strongly associated with metabolic risk factors such as obesity, diabetes mellitus, hypertension, dyslipidemia, and impaired glycemic status. Although mild elevations of liver enzymes may occur, the majority of individuals with NAFLD may present with normal liver enzyme levels. Screening individuals with metabolic risk factors may facilitate early detection and timely intervention to prevent disease progression and associated complications.

Ethical consideration: After ethical clearance from Institutional

Ethical Committee, the participants were included with informed consent for the study.

Declaration of Interest: None.

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