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Elevation of serum alanine aminotransferase and aspartate aminotransferase enzymes level as a predictor of nonalcoholic fatty liver disease in type two diabetic patients

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Abstract

Background: *This is a study of liver function tests in type two diabetic patients reveal that abnormal tests are not uncommon encounter in those in whom their diabetes is poorly controlled and it is regarded as a predictor for non-alcoholic fatty liver disease.*

Aim of this study: *To study the correlation between liver transaminases (alanine aminotransferase and aspartate aminotransferase) and non-alcoholic fatty liver disease in type two diabetic patients.*

Patients and methods: *In this cross sectional study conducted at diabetic and endocrine centre in A-Sadr medical city in Najaf, from February 2014 to March 2015 , a total of 120 type 2 diabetic patients were included (Male 39 and Female 81). Several different factors were studied like age, sex, type of treatment, body mass index and control of diabetes by measuring glycated hemoglobin. Liver transaminases (alanine aminotransferase and aspartate aminotransferase) was done to all those patients and the results are compared with these different factors that mention above. Ultrasonography was done to all the patients searching for any signs of non-alcoholic fatty liver disease like increase in liver size or echogenicity and compared with these factors.*

Results: *Raised Alanine aminotransferase and Aspartate aminotransferase were noted in 20.8% and 16.6% respectively. The mean values of Alanine aminotransferase and Aspartate aminotransferase had no significant correlation with age, sex , mode of therapy or type of diabetes. Values of Alanine aminotransferase and Aspartate aminotransferase were also significantly higher with increasing Body Mass Index. Hepatomegaly, increased liver echogenicity are associated significantly with elevated Alanine aminotransferase and Aspartate aminotransferase values.*

Conclusion*: There was significant correlation between increase level of ALT & AST and the U/S evidence of NAFLD in type 2 diabetic patients. Significant correlation was also found between increase BMI and raise level of liver transaminase ALT & AST) as there was significant association between control of DM and liver transaminase level.*

Keywords: *Non-alcoholic fatty liver disease etc.*

List of abbreviations

Alanine aminotransferase ALT
Aspartate aminotransferase AST
Alkaline phosphatase ALP
Body Mass Index BMI
Cardiovascular Disease CVD
Diabetes Mellitus DM
Glycated Hemoglobin HbA1c
Hepatitis C Virus HCV
Hepatitis B surface Antigen HBs Ag
Liver Function Tests LFTs
Non-alcoholic Fatty Liver Disease NAFLD
Non-alcoholic Steato Hepatitis NASH
Oral Hypoglycemic Drugs OHDs
Prothrombine Time PT
Type 2 Diabetes Mellitus T2DM
Total Serum Bilirubin TSB
Tyroid Stimulating Hormone TSH
Ultrasonography U/S

Introduction

The term diabetes mellitus describes a metabolic disorder with heterogenous aetiologies which is characterized by chronic hyperglycaemia and disturbances of

carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both.

Diabetes mellitus is one of the major non-communicable diseases and the prevalence is rising globally. Type 2 diabetes is the most common form, accounting for 90% of all cases[1]. The prevalence of diabetes worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of diabetes is projected to increase from 171 million in 2000 to 366 million in 2030. Diabetes is more prevalent in men than women[2].

Type 2 DM has been reported to be associated with higher incidence of abnormal liver function tests (LFT)compared to the individuals without diabetes, elevated ALT being the most common abnormality[3].

Glycated hemoglobin

Glycated hemoglobin (HbA1c) is a form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over prolonged periods of time(two to three months). It is formed in a non-enzymatic glycation pathway by hemoglobin's exposure to plasma glucose. Normal levels of glucose produce a normal amount of glycated hemoglobin. As the average amount of plasma glucose increases, the fraction of glycated hemoglobin increases in a predictable way. This serves as a marker for average blood glucose levels over the previous 8 weeks prior to the measurement as this is the half life of red blood cells[4].Good control of diabetes when HbA1c <7 % and poor control when it is >7% [5,6] .

So HbA1c use for control of diabetes during treatment. In diabetes mellitus, higher amounts of glycated hemoglobin, indicating poorer control of blood glucose levels, have been associated with cardiovascular disease, nephropathy, and retinopathy[7].

Alanine & aspartate aminotransferase

Alanine aminotransferase is commonly measured clinically as a part of a diagnostic evaluation of hepatocellular injury, to determine liver parenchymal cell injury. When used in diagnostics, it is almost always measured in international units/liter (IU/L) while aspartate aminotransferase (AST) is similar to (ALT) in that both enzymes are associated with liver parenchymal cells. The difference is that ALT is found predominantly in the liver, with clinically negligible quantities found in the kidneys, heart, and skeletal muscle, while AST is found in the liver, heart (cardiac muscle),skeletal muscle, kidneys, brain, and red blood cells. As a result, ALT is a more specific indicator of liver inflammation than AST, as AST may be elevated also in diseases affecting other organs, such as myocardial infarction, acute pancreatitis, acute hemolytic anemia, severe burns, acute renal disease, musculoskeletal diseases, and trauma[8,9].

Liver plays a major role in the regulation of carbohydrate homeostasis. Hepatocellular glycogen accumulation leads to hepatomegaly and liver enzyme abnormalities in poorly controlled diabetes patients. In hyperglycemic states , there will be intracellular glycogen accumulation in the hepatocytes due to increased glycogen synthesis , causing typical biochemical findings of mild to moderately elevated aminotransferases ,normal liver synthetic function with or without mild elevation of alkaline phosphatase. All these biochemical disturbances and hepatomegaly are found to be reversible with good glycemic control[10].

Non-alcoholic fatty liver disease

Liver can be affected by steatosis or accumulation of fat, a condition known as NAFLD. It is a well-recognized complication of diabetes with frequency of 40-70%[11]. Associated obesity is a confounding variable for fatty liver. Increased transport of fatty acids to the liver, enhanced hepatic fat synthesis as well as decreased oxidation or removal of fat from the liver lead to fat accumulation in the liver.

The steatosis is either microvesicular or macrovesicular and is found to progress to fibrosis and cirrhosis. The most common clinical finding is hepatomegaly, with normal or only mildly elevated transaminases and normal bilirubin[11].

Non-alcoholic fatty liver disease is the main cause of chronic liver disease associated with diabetes and obesity. It was first reported in 1980's in obese females with diabetes. Without treatment, compensated steatosis in NAFLD will eventually lead to decompensated steatosis with necroinflammation and fibrosis, i.e stage of NASH. Non-alcoholic steatohepatitis is a leading cause of end-stage liver disease and also a contributor of cardiovascular disease in type 2 diabetes mellitus[12].

Non-alcoholic fatty liver disease is one cause of a fatty liver, occurring when fat is deposited (steatosis) in the liver not due to excessive alcohol use. It is related to insulin resistance and the metabolic syndrome and may respond to treatments originally developed for other insulin-resistant states(e.g. diabetes mellitus type 2) such as weight loss, metformin and thiazolidinediones[13].

Non-alcoholic steatohepatitis is the most extreme form of NAFLD, and is regarded as a major cause of cirrhosis of the liver of unknown cause [14] .

Non-alcoholic fatty liver disease is considered to cover a spectrum of disease activity. This spectrum begins as fatty accumulation in the liver (hepatic steatosis). The liver can remain fatty without disturbing liver function, but by varying mechanisms and possible insults to the liver may also progress to become NASH, a state in which steatosis is combined with inflammation and fibrosis (steatohepatitis). Non-alcoholic steatohepatitis is a progressive disease: over a 10-year period, up to 20% of patients with NASH will develop cirrhosis of the liver, and 10% will suffer death related to liver disease [15] .

Epidemiology of non-alcoholic fatty liver disease

The prevalence of NAFLD ranges from 9 to 36.9% of the population in different parts of the world [16,17,18] . Approximately 20% of the United States population suffers from non-alcoholic fatty liver, and the prevalence of this condition is increasing[19].The prevalence of non-alcoholic fatty liver disease is higher in Hispanics, which can be attributed to high rates of obesity and type 2 diabetes in Hispanic populations[20].Non-alcoholic fatty liver disease is also more common among men than women in all age groups until age 60, where the prevalence between sex equalize. This is due to the protective nature of estrogen[21].

Diagnosis of non-alcoholic fatty liver disease

Definitive diagnosis of NASH requires liver biopsy[12].Serum amino transferases such as ALT and AST indicate the concentration of hepatic intracellular enzymes that have leaked into the circulation. These are the markers for hepatocellular injury and are used as primary screening of NASH[22].

In a study done in United States by Erbey et al in 2000, the prevalence of elevated ALT among type 2 diabetes is 7.8% compared to 3.8% in those without diabetes[23]. In another study by Salmela *et al*, elevated ALT in diabetes patients was associated with increased BMI and poor glycemic control in multivariate analysis[24].Elevated liver enzymes are found to be predictors of future cardiovascular disease in some studies. In the Firenze Bagno a Ripoli (FIBAR) study done in Italy, raised gamma-GT of more than 40 U/L and AST of more than 40 U/L were associated with increased incidence of Cardiovascular Disease (CVD)[25].

However, subsequent reviews conclude that diagnosis of NAFLD is insufficient to consider as high risk for CVD. The presence of NAFLD should prompt for screening of diabetes, but CVD screening should be guided by other established cardiovascular risk factors[26].

Non-invasive diagnostic tests have been developed, such as FibroTest, that estimates liver fibrosis[19],and SteatoTest, that estimate steatosis[27,28],however their use has not been widely adopted[29]. Apoptosis has been indicated as a potential mechanism of hepatocyte injury as caspase-cleaved cytokeratin 18; however, as the role of oncotic necrosis has yet to be examined it is unknown to what degree apoptosis acts as the predominant form of injury[30,31].

Abdominal ultrasound (US) is widely used for screening asymptomatic patients with an incidental elevation of liver enzymes. However, US cannot detect small amounts of hepatic steatosis and cannot establish the diagnosis of NASH or stage of hepatic fibrosis.

Ultrasonography is currently the most common method for screening asymptomatic patients with elevated liver enzymes and suspected NAFLD. US findings of fatty liver include hepatomegaly, diffuse increases in the echogenicity of the liver parenchyma, and vascular blunting. Nonsteatotic hepatic parenchyma exhibits an echotexture similar to that of renal parenchyma, but becomes ''brighter'' when infiltrated with fat [32] . This hepatorenal contrast can be used for detecting hepatosteatosis [32, 33] . A recent study by Palmentieri *et al*. of 235 patients undergoing US with liver biopsy showed a sensitivity, specificity, PPV, and NPV of 91%, 93%, 89%, and 94%, respectively, for predicting at least 30% steatosis. However, bright liver contrast was not associated with fibrosis in this study[34].

Ultrasonography is easily performed and has a low cost, but it also has some limitations. It is operator dependent and subject to significant intra- and interobserver variability [35] . It is impossible for US to provide quantitative information about the degree of fat accumulation. The sensitivity of US to detect steatosis decreases with a degree of fat infiltration less than 30% [36] . In obese patients, sensitivity lower than 40% has been reported to detect hepatosteatosis[37]. Finally, US has failed to prove efficacious for the detection of inflammation and fibrosis, therefore, it cannot be utilized to diagnose NASH and hepatic fibrosis [38] . In a recent study, however, Iijima *et al*. used an ultrasound contrast agent (Levovist; Sherling, Berlin) to distinguish between simple steatosis and NASH. Levovist contains galactose and palmitic acid and is taken up by hepatocytes[39]. These moieties participate in the sugar and fat metabolism[40]. The uptake of Levovist is observed to significantly decrease in NASH patients, thus correlating with fibrosis rather than steatosis[39]. Larger studies are needed to evaluate contrast US for use in the diagnosis of NASH and advanced fibrosis.

Other diagnostic tests are available. Relevant blood tests include erythrocyte sedimentation rate, glucose, albumin, and renal function. Because the liver is important for making proteins used in coagulation some coagulation related studies are often carried out especially the INR (international normalized ratio). Blood tests (serology) are usually used to rule out viral hepatitis (hepatitis A, B, C and herpes viruses like EBV or CMV), rubella, and autoimmune related diseases. Hypothyroidism is more prevalent in NASH patients which would be detected by determining the TSH[41].

It has been suggested that in cases involving overweight patients whose blood tests do not improve on losing weight and exercising that a further search of other underlying causes be undertaken. This would also apply to those with fatty liver who are very young or not overweight or insulin-resistant. In addition those whose physical appearance indicates the possibility of a congenital syndrome, have a family history of liver disease, have abnormalities in other organs, and those that present with moderate to advanced fibrosis or cirrhosis[42] .

Treatment of non-alcoholic fatty liver disease

A large number of treatments for NAFLD have been studied. While many appear to improve biochemical

markers such as alanine transaminase levels, most have not been shown to reverse histological abnormalities or reduce clinical endpoints[13].

Nutritional counseling

Diet changes have shown significant histological improvement[43]. Specifically, avoiding food containing high-fructose corn syrup and trans-fats is recommended [44].

Weight loss

Gradual weight loss may improve the process in obese patients; rapid loss may worsen NAFLD. Specifically, walking or some form of aerobic exercise at least 30–45 minutes daily is recommended[45].The negative effects of rapid weight loss are controversial. The results of a meta-analysis showed that the risk of progression is very low[45].

A recent meta-analysis presented at the Annual Meeting of the American Association for the Study of Liver Diseases (AASLD) reported that weight-loss surgery leads to improvement and or resolution of NASH in around 80% of patients [46] .

Drugs

Insulin sensitisers (metformin[47] and thiazolidinediones[48]) have shown efficacy in some studies. Vitamin E: Vitamin E can improve some symptoms of NASH and was superior to insulin sensitizer in one large study. In the Pioglitazone versus Vitamin E versus Placebo for the Treatment of Nondiabetic Patients with Nonalcoholic Steatohepatitis (PIVENS) trial, for patients with NASH but without diabetes mellitus, the use of very high dosages of vitamin E (800 IU/day) for four years was associated with a significantly higher rate of improvement than placebo (43% vs. 19%) in the primary outcome.

The primary outcome was an improvement in certain histological features as measured by biopsy—but it did not improve fibrosis.

Pioglitazone, an insulin sensitizer, improved some features of NASH but not the primary outcome, and resulted in a significant weight gain (mean 4.7 kilograms) which persisted after pioglitazone was discontinued[49].

Statin: Improvements in liver biochemistry and histology in patients with NAFLD through treatment with statins have been observed in numerous cases, although these studies were carried out on a relatively small sample of patients[50].Statins have also been recommended for use in treating dyslipidemia for patients with NAFLD.

Modest wine drinking: In a study using the NHANES III dataset, it has been shown thatmild alcohol consumption (one glass of wine a day) reduces the risk of NAFLD by half[51].

Aim of the study

To study the correlation between liver transaminases (alanine aminotransferase and aspartate aminotransferase) and non-alcoholic fatty liver disease in type two diabetic patients.

Patients and Methods

Study design and Subjects

This study was a hospital based cross sectional descriptive study conducted at diabetic clinic of Al-Sadr medical city, Najaf, Iraq from February 2014 to march 2015. Subjects were recruited according to simple random sampling method meeting the selection criteria.

Selection Criteria

Inclusion Criteria

The patients with confirmed diabetes mellitus, fasting plasma venous glucose of ≥ 7 mmol/l (126 mg/dl) or random or two hour post prandial plasma venous glucose of ≥ 11.1 mmol/l (200 mg/dl).

Exclusion Criteria

1. History of alcohol intake.
2. Use of hepatotoxic drugs like amiodarone, antituberculous drugs.
3.History of liver diseases (Wilson disease, hemochromatosis , autoimmune liver disease) or clinical evidence of acute hepatitis.
4.Those who were found to have evidence of hepatitis B and C virus infection (HBsAg positive and HCV antibody positive),EBV & CMV.
5.Inflamatory bowel disease.
6.Human immune deficiency virus.
7.Pregnency.

Ethical Considerations

The Institution's Ethical Committee approval was obtained prior to the enrolment of subjects. The objectives and the detailed procedures of blood taking and imaging involved in the study were explained to all eligible subjects for this study. Emphasis was given that participation in this study was voluntary.

Questionnaire and Bio data Collection

A questionnaire was specifically designed to obtain information which helps to select individuals according to the selection criteria of the study. The questions also focused on sociodemographic data (age,sex)and background characteristics of diabetes(family history of diabetes, mode of anti-diabetic therapy).Weight and height were measured using standard procedures and

(BMI)was then calculated from the formula of weight(kg)/height(m^2).

Blood Sample

Five ml of venous blood was drawn from each volunteer in this study using a disposable plastic syringe. The sample was then analysed for ALT, AST by 550 Expressed Plus Automatic Chemistry Analyzer at the laboratory department of Al-Sadr medical city.

Imaging of Liver

Ultrasonographic examination of abdomen was carried out at the radiology department of Al-Sadr medical city to determine the size, echogenicity of liver.

Statistical Analysis

By using the statistical package for social sciences (SPSS) software for windows, version 20, data of all participants were entered and analyzed with appropriate statistical tests.

Descriptive statistics were presented as mean ± for age, ALT & AST level, BMI, as frequencies (number) and percentages (%).

Chi square test (X^2) was used to compare frequencies of categories variables.

Level of significance (P.value) of ≤ 0.05 indicated a significant difference or correlation.

Results

Table 1 Demographics and clinical parameters of diabetic patients (n=120)

Variable		N(%)
Age	<55	49(40.8%)
	>55	71(59.2%)
Sex	Male	39(32.5%)
	Female	81(67.5%)
Type of treatment	Insulin	11(9.1%)
	OHDs	109(90.9%)
BMI	<25	24(20%)
	>25	96(80%)
HbA1c	<7%	60(50%)
	>7%	60(50%)

Table 2 Mean value of biochemical markers among diabetic patients

Variable	Mean	Laboratory reference	No. of patients outside the reference
ALT	42.94	0-55 IU/L	25(20.8%)
AST	29.69	5-34 IU/L	20(16.6%)

Table 3 The number of diabetic patients with abnormal liver U/S regarding size, echogenicity

Liver U/S	Size	Normal	98(81.6%)
		Increase	22(18.4%)
	Echogenicity	Normal	92(76.6%)
		Increase	28(23.4%)

Table 4 The relation between ALT & AST level and different clinical parameters in diabetic patients

Variable		total	Normal ALT	High ALT	P-Value	Normal AST	High AST	P-value
Age	<55	49	40	9	0.580	41	8	0.933
	>55	71	55	16		59	12	
Sex	Male	39	31	8	0.952	34	5	0.615
	Female	81	64	17		66	15	
Type of treatment	Insulin	11	10	1	0.314	8	3	0.321
	OHDs	109	85	24		92	17	
Control of DM(HbA1c)	<7%	60	55	5	0.001*	56	4	0.003*
	>7%	60	40	20		44	16	
BMI	<25	24	23	1	0.024*	24	0	0.014*
	>25	96	72	24		76	20	

*significant association

In table 4 we see that there is significant association in ALT & AST in those with poor control of DM and also there is significant association in those with high BMI.

Table 5 The relation between abnormal ALT level and glycemic control in patients with high BMI

	Normal ALT	High ALT	Total	P Value
BMI > 25 HbA1c > 7%	27	15	42	0.032*
BMI > 25 HbA1c < 7%	45	9	54	

*significant association

Table 6 The relation between abnormal AST level and glycemic control in patients with high BMI

	Normal AST	High AST	Total	P Value
BMI > 25 HbA1c > 7%	26	16	42	0.001*
BMI > 25 HbA1c < 7%	50	4	54	

*significant association

Table 5,6 show the significance of high ALT & AST level in those with high BMI and poor glycemic control.

Table 7 The relation between U/S finding of liver size, liver echogenicity with different clinical parameters in diabetic patients

Variable		Total	Normal liver size	Increase liver size	P-Value	Normal liver echogenicity	Increase liver echogenicity	P-Value
Age	<55	49	37	12	0.147	39	10	0.529
	>55	71	61	10		53	18	
Sex	Male	39	33	6	0.562	28	11	0.381
	Female	81	65	16		64	17	
Type of treatment	Insulin	11	9	2	0.989	9	2	0.671
	OHDs	109	89	20		83	26	
Control of DM(HbA1c)	<7%	60	54	6	0.018*	53	7	0.002*
	>7%	60	44	16		39	21	
BMI	<25	24	23	1	0.044*	23	1	0.013*
	>25	96	75	21		69	27	

*significant association

Table 8 The relation between liver echgenicity and glycemic control in patients with high BMI

	Liver echogenicity			
	normal	increase	total	P Value
BMI > 25 HbA1c > 7%	25	17	42	0.017*
BMI > 25 HbA1c < 7%	44	10	54	

*significant association

Table 9 The relation between liver size and glycemic control in patients with high BMI

	Liver size			
	normal	increase	total	P Value
BMI > 25 HbA1c>7%	47	7	42	0.016*
BMI > 25 HbA1c<7%	28	14	54	

*significant association

A total of 120 confirmed diabetes patients participated in this study. Table 1 shows demographic and clinical characteristics. Mean age was 52 ± 8 years and ranged from 40 years to 65 years. Male represented 32.5% of the cases while female represented 67.5% .(Table. 1).

Mean BMI was 25.84, ranging from 22.5 to 30.5. Ninty point nine percent were treated with OHA(Table.1). the mean of ALT & AST was 42.94 & 29.69 respectively(Table.2). Regarding clinical characteristics, only 18.4% of the patients had increased liver size, 23.4% had increased liver echo (Table.3).

The AST & ALT levels were significantly higher among the patients with poor glycemic control compared to those with good glycemic control (p = 0.001 & 0.003 respectively) , (Table 4). Significant association also found in level of ALT & AST with the increase in BMI(P=0.024 & 0.014 respectively)(Table 4).

When we take those with high BMI we see that ALT & AST level significantly increase with poor glycemic control (p=0.032 & 0.001 respectively)(Table 5,6).

Increase liver size and echogenicity were significantly present among the patients with poor glycemic control compared to those with good glycemic control (p = 0.018 & 0.002 respectively), (Table 7). Significant association also found with the increase in BMI (P=0.044 & 0.013 respectively)(Table 7).

When we take those with high BMI we see that U/S signs of fatty changes (increase liver size, increase echogenicity) significantly present with poor glycemic control (p=0.017 & 0.016 respectively) (Table 8,9).

Table 8, 9 show the significance of abnormal liver U/S (increase size, increase echogenicity) in those with high BMI with poor glycemic control.

Discussion

In our study the age was divided into two groups, less than and equal to 55 years and more than 55 years; no significant difference was noted in the means of ALT and AST between these two groups. Likewise, there was no significant difference in mean of ALT between male and female. Means of ALT and AST also not significantly differed between different types of treatment. The mean values of ALT and AST were significantly higher among patients with increased BMI and poor control of DM.

Also we found in our study that there is significant association between the level of ALT & AST in those with high BMI and the poor glycemic control at same time.

In our study we found also that there is no significant difference was noted in the liver size & its echogenicity between these two groups & there was no significant difference between male and female. Liver size & its echogenicity also not significantly differed between different types of treatment but it significantly higher among patients with increased BMI and poor control of DM.

Also we found in our study that there is significant association between increase liver size & increase its echogenicity in those with high BMI and the poor glycemic control at same time.

Salmela *et al* in 1984 studied the liver function tests of 175 diabetic patients without chronic liver disease, where 57% were found to have at least one abnormal LFT,27% had at least two abnormal LFTs. However, these increases in liver function values were rarely more than two times of the upper limit of normal [24].

A cross sectional study from Iran demonstrated a rise of ALT in 10.4% and AST in 3.3% of type 2 diabetes patients[22].In a UK cohort study of 959 diabetic patients over four year period, 15.7% had raised ALT, 10.4% had elevated alkaline phosphatase whereas only 3.9% had hyperbilirubinaemia[52]. Another study of 60 well controlled diabetic outpatients showed elevation of alkaline phosphatase and γGT in 11 and 10 patients respectively, but the rise was not more than two times upper limit of normal value [53].

According to a study in Sudan, where 50 diabetes patients and 30 normal control subjects were tested for liver function, the means of ALT , AST , γGT, total protein and albumin were reported to be significantly higher among diabetes compared to the control[55]. In this study, 22% had at least one abnormal liver function test.

Abnormal liver function tests in diabetes patients can be attributed to several factors, the most common cause being NAFLD associated with insulin resistance and metabolic syndrome in diabetes. Recently, studies have revealed the association of hepatitis C virus infection in diabetes patients causing deranged LFTs [56]. Though relatively infrequent, statin therapy can also contribute to abnormal liver function results [3].

Majority of the studies on liver function in diabetes excluded the hepatotoxic causes of viral hepatits, alcohol and medications. These studies focused on the factors influencing the liver function in diabetes.

Elevated ALT was significantly associated with overweight, poor glycemic control and those treated with diet control or oral agents on multivariate analysis according to Salmela *et* al.

Contrary to the above study, Foster *et al* reported no significant correlation between measures of glucose control and abnormal liver function tests. However, they found that presence of abnormally bright liver echo on ultrasound imaging was associated with minimally elevated ALT and AST. This bright liver echo was due to fatty infiltration of liver [53].

Like to our study Sadiq Jabbar Al-Muhana *et al* found that there is a significant association between fatty liver on ultrasound and abnormal liver function tests [54].

Among the Iran diabetes population, although raised ALT was seen with increasing age, fasting blood glucose and triglyceride levels, it was not statistically significant. The incidence of high AST was more common among men [22].

Erbey JR et al reported that the prevalence of elevated ALT levels among the U.S. type 2 diabetics was 7.8% and this prevalence was higher among obese (BMI > 25kg/m^2) than non-obese diabetics (10.6% vs . 6.6%)[23].In Sudan, high serum alanine aminotransferase level is greater among type 2 diabetes , overweight or obese and men[55].

The elevated ALT levels were significantly related to a BMI of > 25 kg / m^2 among the type 2 diabetics (p=0.0103) in a study conducted in India. Positive correlation was also reported between glycaemic control and duration of diabetes mellitus with the ALT levels in this Indian study [57].

According to a study in India, age, duration of diabetes, presence of hypertension, family history of diabetes mellitus, body mass index, waist circumference, treatment with Metformin, and prevalence of metabolic syndrome were similar between diabetes patients with and without nonalcoholic steatohepatitis (NASH)[58].

Similarly, in our study, no significant correlation was noted between means of ALT and AST with age, mode of therapy. Mean ALT had no correlation with sex of the population. Values of ALT and AST were also significantly higher with increasing BMI.

A large cohort study done in India reported the presence of fatty infiltration of liver in ultrasonography in 62.25 %(127 out of 204 diabetes patients) [58]. Our study revealed presence of increase liver echogenicity in 23.4% of diabetes patients on ultrasound scan.

Raised liver enzymes can be a marker of steatohepatitis in diabetes patient. Nevertheless, evidence fails to show significant positive correlation between liver histology and biochemical derangement [24, 58].Advanced degree of NASH and fibrosis can occur in diabetic patients without significant liver function abnormalities [58].

In the present study, means of ALT and AST were significantly correlated with hepatomegaly, increased liver echogenicity on ultrasound imaging. This might be due to the presence of nonalcoholic steatohepatits in these patients. However, exact confirmation will require histological examination which is invasive.

Conclusion

There was significant correlation between increase level of ALT & AST and the U/S evidence of NAFLD in type 2 diabetic patients.

Significant correlation was also found between increase BMI and raise level of liver transaminase (ALT & AST) as there was significant association between control of DM and liver transaminase level.

Based on the findings of this study, raised ALT and AST are more common among the diabetes patients with higher BMI and those with poorly controlled Diabetes. Derangement of liver enzymes correlated statistically significantly with fatty liver on ultrasound. Therefore, abnormal liver function tests among poorly controlled diabetic patients can be indicator of associated nonalcoholic fatty liver disease.

Recommendations

Checking for liver enzymes, ALT and AST should be carried out to screen the possibility of underlying fatty liver, which might need further evaluation and early intervention to prevent progression into cirrhosis and chronic liver disease, especially in poorly controlled type 2 DM patients with high BMI.

Larger studies are recommended in future to find out the exact association between the biochemical and histological changes of liver in diabetes patients without chronic liver pathology.

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