

## FREQUENCY OF NON ALCOHOLIC FATTY LIVER DISEASE (NAFLD) AND ITS BIOCHEMICAL DERANGEMENTS IN TYPE-2 DIABETIC PATIENTS

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### ABSTRACT

**Objective:** To see the frequency of non-alcoholic fatty liver disease in Type-2 diabetic patients and to see biochemical derangements in NAFLD patients.

**Methodology:** It is a cross-sectional study, conducted at Diabetic Research Centre & outpatient department Nishtar Hospital and PMRC Research Centre Nishtar Medical College, Multan. One hundred patients of either sex having type 2 diabetes mellitus attending diabetic out-patient department Nishtar Hospital Multan were included in the study. A pre-designed study pro forma was filled with relevant investigations and clinical assessments were carried out in all cases. All the patients underwent abdominal ultrasonography. Data were entered in SPSS-11 & analyzed.

**Results:** Out of one hundred patients, 51 (51%) were female and 49 (49%) were male. Mean age of the patients was 47.93±8.57 years. Fifty one (51%) of the diabetic patients had fatty liver. Out of these 32 (62.75%) were female and 19 (37.25%) were male. Fatigue was present in 49 (53.26%), generalized weakness in 48 (52.18%), heaviness right upper abdomen in 22 (64.70%) and pain right upper abdomen in 20 (58.82%) of fatty liver patients. Corresponding figure in Non Fatty Liver Patients were 43 (46.74%), 44 (47.82%), 12 (35.30%) & 14(41.18%), respectively. Itching was noted in 19 (44.18%) patients of fatty liver while it was 24(55.82%) in non-fatty liver patients. Serum triglyceride level more than 160 mg/dl in 47 (92.15%) patients of fatty liver while serum cholesterol level more than 200mg/dl was seen in 24(47.05%). Aspartate amino transferase (AST) more than 35 u/l was noted in seven (13.72%), alanine amino-transferase (ALT) more than 40u/l was noted in 6(11.76%) fatty liver patients while serum albumin and serum billirubin were within normal range in all fatty liver and non-fatty liver patients.

**Conclusion:** Nonalcoholic fatty liver disease (NAFLD) is more commonly seen in Type-2 diabetic patients. Serum triglyceride and serum cholesterol are significantly raised in NAFLD patients. Raised ALT and AST was not a common finding in our NAFLD study patients. Diabetic patients having heaviness or pain right upper abdomen with raised serum triglycerides and cholesterol should be more closely observed for NAFLD and liver complications.

**KEYWORDS:** Non-alcoholic fatty liver disease (NAFLD), Type-2 diabetes mellitus.

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### INTRODUCTION

Fatty liver is a problem which is commonly encountered in medical practice. It is defined as diffused accumulation of fats mainly triglycerides in the liver cells. Usually the fat contents increase more than 5% of the normal liver

weight.<sup>1</sup> If there is only accumulation of fats it is called steatosis and when this fat accumulation is accompanied by necro-inflammatory changes in the liver it is called steato-hepatitis. Fatty liver is divided mainly into two categories, i.e. 1. Alcoholic fatty liver a and 2. Non-alcoholic fatty liver.

The term non-alcoholic fatty liver disease (NAFLD) includes spectrum of changes from steatosis alone to non-alcoholic steato-hepatitis. Diabetes mellitus is an important cause of NAFLD while other important causes are obesity, hepatitis B, hepatitis C virus infection, pregnancy and certain drugs especially amiodarone, synthetic estrogens, cortico-steroids and tamoxifen. NAFLD is also seen in patients with Wilson's disease and haemo-chromatosis. It occurs when more fat is transported to liver from other parts of the body especially intestine, when accumulation of fats exceeds than its degradation and when excess carbohydrates is delivered to the liver are converted into fatty acids. Hence they are incorporated into triglycerides and are retained in hepatocytes. Liver damage is produced due to accumulation of fats, oxidative stress of mitochondria and by release of inflammatory cytokines.

In diabetics NAFLD is usually associated with metabolic syndrome which is characterized by insulin resistance, obesity, hypertriglyceridemia and hypertension and some studies describe NAFLD as hepatic component of metabolic syndrome.<sup>2</sup> Various studies have reported variable prevalence rates of NAFLD in general population and in diabetic patients.<sup>2-7</sup> It can occur at any age but mostly seen in age group of 40-60 years. It is commonly seen in obese persons and truncal obesity is main culprit. Fatty liver is usually asymptomatic but patients may present with fatigue, generalized weakness, jaundice, nausea, vomiting, loss of appetite, un-explained weight loss and itching. In advance stage patient can present with stigmata of chronic liver disease. Various biochemical derangements have also been described in NAFLD patients.<sup>8</sup> The definite diagnosis is based upon histological examination of liver tissue however it is an invasive and costly procedure and is associated with complications. The

present study was designed to see the frequency and biochemical derangements of NAFLD patients in Type-2 diabetics.

## METHODOLOGY

It was a cross-sectional study which was done using non-probable purposive sampling. A total of one hundred Type-2 diabetic patients were randomly selected from diabetic out patient department at Nishtar Hospital Multan. Informed verbal consent was taken from each patient and pre-designed pro forma was filled in. Alcoholics and anti-HCV positive patients were excluded from the study.

The presenting complaints of the patients were recorded and clinical assessment was done. All the patients underwent abdominal ultrasonography for detection of fatty liver by a sonologist. Serum cholesterol, serum triglycerides, ALT, AST, serum alkaline phosphatase, serum albumin, serum billirubin and anti-HCV were done in all the cases. The data were entered and analyzed using computer program SPSS-11.

## RESULTS

A total of one hundred diabetic patients were studied. Out of these, 51(51%) were female and 49 (49%) were male. Age varied from 40-70 years and mean age of the patients was  $47.93 \pm 8.57$  years. Fifty one (51%) of these patients had fatty liver. Out of these 51 patients, 32 (62.75%) were female and 19 (37.25%) were male. Patients presented with various complaints as shown in Table-I. The major complaints were fatigue, generalized weakness and itching. Serum albumin and serum billirubin were normal in all the study patients while other biochemical derangements in NAFLD patients are given in Table-II.

## DISCUSSION

Non-alcoholic fatty liver disease (NAFLD) is a common liver disorder. It is mainly seen in obese and diabetic patients. Varying prevalence rates have been reported in various studies. A recent study from Japan in apparently healthy individuals has reported the prevalence of NAFLD as 29%.<sup>3</sup> An Italian study reported it to

Table-I: Presenting complaints of fatty and non-fatty liver diabetic patients.

Complaints	Fatty liver patients	Non-fatty liver patients	P-value
Fatigue	49 (53.26%)	43 (46.74%)	0.77
Generalized weakness	48 (52.18%)	44 (47.82%)	0.78
Heaviness right upper abdomen	22 (64.70%)	12 (35.30%)	0.01
Pain right upper abdomen	20 (58.82%)	14 (41.18%)	0.21
Itching	19 (44.18%)	24 (55.82%)	0.23
Nausea	15 (60.00%)	10 (40.00%)	0.29
Anorexia	08 (53.34%)	07 (46.66%)	0.84

be 20%.<sup>4</sup> The frequency of NAFLD reported in general population of USA is 20%.<sup>5</sup> A study from Karachi, Pakistan conducted by Luxmi et al,<sup>2</sup> in 120 diabetic patients described the frequency of NAFLD as 60.8% and Akber et al from Saudi Arabia as 55%<sup>6</sup> in Type-2 diabetics. Gupta et al from India report it to be 49% in diabetics.<sup>7</sup>

In present study frequency of NAFLD is 51% which is close to the finding from India and Pakistan. It is pertinent to say that we have taken abdominal ultrasonography as a tool for detection of NAFLD which can only detect if the fat content of the liver is more than 33% and sensitivity of ultrasonography for detection of fatty liver is poor if the patient has fat content less than 33% of the liver weight. The frequency of NAFLD actually might have been high if we had done liver biopsy for the diagnosis of NAFLD.

Various studies describe NAFLD as asymptomatic which may be true in initial phase of NAFLD but patients may present with fatigue and heaviness in right upper abdomen later on. In present study fatigue was noted as chief complaint in 92 diabetics, out of these 49 (53.26%) were fatty liver patients. Generalized weakness was seen in 92, out of which 48 (52.18%) were having NAFLD. Here it is difficult to say whether these complaints were purely due to NAFLD or underlying diabetes mellitus as our study population was type 2 diabetic patients.

Heaviness right upper abdomen 22 (64.70%) and pain right upper abdomen 20 (58.82%) was seen in fatty liver patients. A study by Wingkin syn et al described fatigue as an important symptom and pain right upper abdomen in 33% of the patients.<sup>9</sup> Heaviness and pain in right upper abdomen is due to stretching of the liver capsule which is correlated with the amount of fat present in the liver.<sup>8,10</sup> Diabetes mellitus is an important risk factor for NAFLD. It is established that diabetes mellitus through insulin resistance leads to increased free fatty acid load to the liver consequently high triglyceride synthesis and increased secretion of triglyceride rich very low density lipoprotein by the liver. Hyper-triglyceridemia is strongly correlated with NAFLD and our study also supports this. Serum triglycerides were raised in 92.15% of fatty liver patients. Similarly serum cholesterol was raised in 47.05% of patients. The study by Luxmi et al<sup>2</sup> also reported raised serum triglyceride level in patients with fatty liver and same is the result from our study.

Serum alkaline phosphatase was raised in 15.68% of our study patients. Raised Alkaline phosphatase has been described in fatty liver patients especially in old females.<sup>11</sup> AST and ALT were raised in our study in only seven (13.72%) and six (11.76%) fatty liver patients respectively, however raised ALT and AST have

Table-II: Biochemical profile of fatty and non fatty liver diabetic patients

Investigations	Fatty liver patients	Non-fatty liver patients	P-value
Serum Triglycerides(more than 150 mg/ dl)	47	39	0.65
Serum Cholesterol(more than 200 mg/dl)	24	18	0.18
Serum Alkaline Phosphatase (more than 306 u/l)	08	05	0.21
AST(more than 35 u/l)	07	04	0.23
ALT(more than 40u/l)	06	06	NA

been reported in significant number of fatty liver patients in other studies.<sup>12,13</sup> Raised ALT level is important finding in fatty liver patients<sup>1</sup> while raised ALT was not seen in significant number of NAFLD patients in our study and these findings support the study by Luxmi et al.<sup>2</sup> Normal ALT has also been reported in NAFLD by other studies.<sup>9</sup> Mofrad<sup>14</sup> reported that histologic spectrum is not significantly different in patients with the raised or normal ALT and normal values did not confirm freedom from steato-hepatitis.

### CONCLUSION

Nonalcoholic fatty liver disease (NAFLD) is more commonly seen in Type-2 diabetic patients. Serum triglyceride and serum cholesterol are significantly raised in NAFLD patients. Raised ALT and AST is not a common finding in our NAFLD study patients. Diabetic patients having heaviness or pain right upper abdomen with raised serum triglycerides and cholesterol should be more closely observed for NAFLD and liver complications.

#### *Suggestions:*

1. Type 2 diabetic patients should also be monitored for the development of NAFLD and its complications.
2. Anti-HCV positive Type-2 diabetic patients having fatty liver should be more carefully looked for sequelae of fatty liver.

*Limitations of the study:* We could not do liver biopsy due to ethical and financial constraints. Sample size was also small due to financial constraints.

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