Original Article

NAFLD in Diabetics

Frequency of Nonalcoholic Fatty Liver Disease (NAFLD) in Diabetes Mellitus (DM) Type–II Patients

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ABSTRACT

Objectives: To assess the frequency of nonalcoholic fatty liver disease (NAFLD) in diabetes mellitus (DM) type –II patients.

Study Design: Observational study.

Place and Duration of Study: This study was conducted at the Department of Medicine, Dow University Health Sciences and Chiniot General Hospital Karachi from 18th August 2015 to 17th May 2016.

Materials and Methods: All diabetic type –II patients since 5 years, aged > 20 years were screened for nonalcoholic fatty liver disease attending medical outpatient clinic. Take a history was regarding alcohol use. Patient having a history of alcohol consumption, chronic liver disease of any cause and intake of hepatotoxic drugs were excluded .All patients plain fro ultrasonography for assessment of non alcoholic fatty liver. The data was entered and analyzed using SPSS version 20.0.

Results: 387 cases Diabeties Mellitus-II since 5 years. Female patients were mostly presented with DM-II in 272(70.28%) female, female to male ratio were 2.36:1. The mean age was 41+2.17years. Mostly patients reported in 4th and 5th decade age groups 299(77.26%) cases in between 40-60 years. Grade-I nonalcoholic fatty liver disease was 42(10.85%) cases more reported as compare Grade-II and Grade -III. Frequency of nonalcoholic fatty liver disease on ultrasonography were observed in 72 (18.60%) cases.

Conclusion: Patients with type II diabetes along with NAFLD are at significantly increased risk of cardiovascular, cerebrovascular and peripheral vascular disease than general population.

Key Words: Nonalcoholic Fatty Liver Disease, Diabetes Mellitus, Type-II.

Citation of article: Mobin A, Shaikh H, Manzoor I, Khan MU. Frequency of Nonalcoholic Fatty Liver Disease (NAFLD) in Diabetes Mellitus (DM) Type–II Patients. Med Forum 2017;28(4):22-25.

INTRODUCTION

The rise in obesity and other metabolic disorders have made NAFLD a common pathology. It is the most common cause of elevated liver enzymes. Its prevalence is very high in diabetics; 70% in diabetic patients as compared to 20% in general population. Many patients with NAFLD are asymptomatic with normal liver function tests (LFTs). It is suspected clinically when routine laboratory investigations reveal increased transaminases with ALT levels being greater than AST. In alcoholic liver disease, AST is greater than ALT because AST is found within the mitochondria which is eventually destroyed by alcohol. With progression of disease AST levels rise higher and increase the AST to ALT ratio. Progressive rise in AST levels demonstrate progression to non-alcoholic steatohepatitis (NASH) and fibrosis[1].

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Received: February 10, 2017; Accepted: March 15, 2017

Despite this, there has been no association between ALT levels and severity of NAFLD. Also the presence of normal levels of aminotransferases does not exclude the diagnosis of fatty liver[2]. The Dallas Heart Study shows 79% patients with hepatic steatosis having normal ALT levels. Another study demonstrates 86% patients with NAFLD having normal ALT levels[3]. This is the reason for patients undergoing liver biopsy to detect the level of pathologic damage to the liver[4]. Ultrasonography can also detect NAFLD as increased hepatic echogenecity however this is usually an incidental finding and ultrasound is usually not done for detection of NAFLD because of its poor sensitivity. The sensitivity of Ultrasound is 100% and CT scan is 93% only in the presence of hepatic fat content greater than 33%. If the hepatic fat content is less than described, the sensitivity of these modalities is diminished. Other laboratory findings may include dearrangement of Gamma Glutamyl-transferase, prolonged prothrombin time, low serum albumin and raised serum bilirubin[5,6].

Insulin resistance in hepatic and extra-hepatic tissues such as adipose tissues account for underlying pathogenesis of NAFLD. The triacyl-glycerols accumulating within the liver comes from three main sources: circulating free fatty acids, from lipogenesis and from dietary lipids [7]. Increased intrahepatic glucose

increases pyruvate levels and hence increased amount of acetyl CoA is converted to malonyl CoA for de novo lipogenesis. Development of steatohepatitis and fibrosis involves inflammatory mechanisms such as oxidative stress, mitochondrial dysfunction and circulating inflammatory mediators. The "hit" hypothessis proposes that fibrosis accounts for failure of hepatocytes to regenerate[8,9]. Insulin resistance leads to dysfunctional adipocytes which release large amount of inflammatory mediators such as TNF-alpha, IL-6 and low quantities of adiponectin. Adiponectin increases fatty acid oxidation and prevents lipid accumulation and inflammation[10].

Histologically NAFLD has been categorized into the following four categories: Type 1 is simple fatty liver, type 2 indicates steatohepatitis, type 3 is steatonecrosis whereas type 4 is presence of hyaline or fibrosis along with steatonecrosis. In majority of cases NAFLD carries a benign course whereas NASH follows and aggressive course and leads to liver cirrhosis[11].

MATERIALS AND METHODS

This study was conducted in medicine department of Dow University Health Sciences and Chiniot General Hospital Karachi, from 18th Aug 2015 to 17th May 2016.

All diabetic type –II patients since 5 years, aged > 20 years were screened for nonalcoholic fatty liver disease attending medical outpatient clinic. Take a history was regarding alcohol use. Patient having a history of alcohol consumption, chronic liver disease of any cause and intake of hepatotoxic drugs were excluded . All patients plain fro ultrasonography for assessment of non alcoholic fatty liver according to grades. The data was entered and analyzed using SPSS version 20.0

RESULTS

Table No.1: Demographic Variable N=387

Variable	No. Patients	Percentage
Gender		
• Male	115	29.31%
• Female	272	70.28%
Age		
• 20-35 years	88	22.73%
• 36-50 years	189	48.83%
• 51-60 years	110	28.42%
Grade of nonalcoholic fatty liver disease Ultrasound Finding		
• Grade-0	315	81.39%
• Grade-I	42	10.85%
• Grade-II	21	5.42%
• Grade-III	9	2.32%

There were diagnosed 387 cases Diabetic Mellitus-II since 5 years. Female patients were mostly presented with DM-II in 272(70.28%) female, female to male ratio were 2.36:1. The mean age was 41±2.17years. Mostly patients reported in 4th and 5th decade age groups 299(77.26%) cases in between 40-60 years. Grade-I nonalcoholic fatty liver disease was 42(10.85%) cases more reported as compare Garde-II and Garde –III(table 1 &2). Frequency of nonalcoholic fatty liver disease on ultrasonography were observed in 72 (18.60%) cases (Chart No.1).

Table No.2: Grades of non alcoholic fatty liver according to sex n=387

Grades of non alcoholic fatty liver	Sex			
	Male (n=115)		Female (n=272)	
	No. Patients	%age	No. Patients	%age
Grade – 0 N=315	77	19.89%	238	61.49%
Grade – I N=42	23	5.94%	19	4.90%
Grade – II N=21	9	2.32%	12	3.10%
Grade – III N=9	6	1.55%	3	0.77%

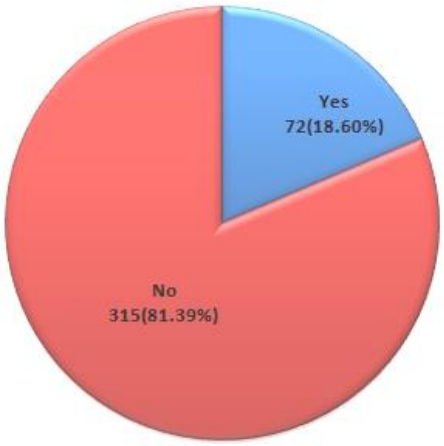

Chart No.1: Frequency of non alcoholic fatty liver disease

DISCUSSION

NAFLD is a wide spectrum of liver pathologies ranging from benign asymptomatic condition to fibrosis and eventually cirrhosis or hepatocellular carcinoma. Risk factors associated with NAFLD include male sex, family history of type II diabetes and certain ethnicities. Mutations in PNP3 gene has been found to be associated with early development of fatty liver. Other rare causes include some drugs such as amiodarone, synthetic estrogens. tamoxifen, diltiazem and highly active anti-retroviral therapy, refeeding syndrome, severe weight loss, lipodystrophy or long term total parental nutrition[1].

It has been seen that the incidence of NAFLD increases with age[12]. The risk factors for NAFLD also increase with age. Amongst these include hypertension, diabetes and dyslipidemias[13]. Elderly with NAFLD have higher

mortality ratio then general population. These patients have higher than usual chances of early progression to severe hepatic fibrosis and hepatocellular carcinoma[14,15]. Elderly with obesity are at much increased risk. Cryptogenic cirrhosis which is also known as burned out NASH is common in obese elderly including those who were obese during younger age[16].

Only few studies suggest that female gender is associated with higher incidence of NAFLD and fibrosis whereas majority of studies support the fact that men have higher incidence of NAFLD. Obesity is a well known risk factor for development of diabetes and metabolic syndrome. Both of these conditions can lead to early development of NAFLD. Females are more prone to obesity and metabolic syndrome. Our study shows 70.28% of females. Study conducted on 26,527 Asians reveal 31% males and 16% females with NAFLD[17]. Another study conducted in India shows greater number of males than females[18]. 81.3% patients had grade 0 histology whereas 10.85% had grade I histology. 5.42% had grade II histology whereas 2.32% had grade III histology. Matteoni et al reports biopsy results of 132 patients with NAFLD. He reports 37% patients with type 1, 7% with type II, 14% with type III and 40% with type IV NAFLD. He reports that female gender was more common in type IV whereas in our study male gender was more common. He concludes that the overall ratio of deaths was similar among all four histologic categories. However cirrhosis and liver related deaths were more among patients with histologic stage 3 and 4 [19].

It has been seen that NAFLD is associated with increased risk of future cardiovascular events among patients with type 2 diabetes mellitus. This increased risk is independent of other risk factors of NAFLD. A cohort study was done in 132 patients with NAFLD. Diagnosis was confirmed by biopsy and the patients were followed upto 18 years. The most common cause of deaths among these patients was liver related problems followed by cardiovascular events and cancer related causes [20].

Co-occurrence of diabetes and NAFLD are associated with more severe outcome then either of these conditions alone. There is evidence suggesting the fact that insulin therapy in beneficial for diabetic patients in terms if NAFLD. The degree of hepatic steatosis was found to be improved after 12 weeks of insulin glargin therapy as measure by MRS[21].

Treatment of patients with diabetes and NAFLD focuses on resolving underlying insulin resistance. This includes life style modifications such as regular exercise, weight loss and dietary modifications. Rapid weight loss should be avoided and it can lead to worsening of NAFLD. It is recommended that weight loss should not exceed more than 2lb per week (d9 ka 16,43) [22]. Alchohol use should be restricted. Pharmacologic therapy includes metformin and thiazolididiones[23]. Metformin can improve insulin sensitivity and improve hepatic fat content. In controlled studies where metformin was used in non-diabetic patients with NAFLD metformin proved to be an effective treatment. However in randmized trials in diabetics with NAFLD, metformin had no effect on hepatic triglyceride content [24]. However using metformin along with insulun therapy was found to be beneficial in normalizing serum transaminase levels and reducing hepatic steatosis[25]. Hepatic triglyceride content was reduced by 45% and reached normal levels in 75% patients with 3 months of insulin therapy along with metformin. In a group of patients with biopsy proven NASH along with insulin resistance or diagnosed type II diabetes, treatment was offered with pioglitazone which brought improvement in ALT levels, hepatic fat content and liver histology However it was observed that there was average weight gain of 2kgs which may be due to redistribution of hepatic fat from liver to adipose tissues [26].

CONCLUSION

Patients with type II diabetes along with NAFLD are at significantly increased risk of cardiovascular, cerebrovascular and peripheral vascular disease than general population. Treatment goals include improving insulin resistance with lifestyle modifications along with pharmacolgic therapy.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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