ORIGINAL ARTICLE

FREQUENCY OF NONALCOHOLIC FATTY LIVER DISEASE IN GENERAL MEDICAL OUT PATIENTS

Saleem Iqbal, Sheema Khan, Muhammad Darwesh Iqbal, Noor ul Iman

Department of Medicine, Khyber Teaching Hospital, Peshawar - Pakistan

ABSTRACT

Objectives: To determine the prevalence of Non Alcoholic Fatty Liver Disease (NAFLD) in patients seen in general medical outpatient department.

Material and methods: This observational prospective study was conducted in General Medical Outpatient Department of Khyber Teaching Hospital Peshawar, from 4th April, 2017 to 4th July, 2017. A total of 2007, patients were reviewed, out of which, 436 patients had NAFLD, as suggested on ultrasound, were included in the study.

Results: Out of 436 patients, 83.02%% were females, 61.46% were in the age range 40-60 years, 80.49% patients were obese as per BMI criterea, 54.81 % had hypertension, 35.77% had T2DM, 43.57% had Serum hypertriglyceridemia, 20.64% had serum hypercholestremia and 41.05 % had elevated Serum ALT level.

Conclusion: Prevalence of NAFLD is increasing in females of age range 40 to 60 years, having higher frequency of obesity, hypertension, T2DM & serum hypertriglyceridemia,

Key words: Non Alcoholic, Fatty Liver, hypertension, Type 2 diabetes mellitus, metabolic syndrome.

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INTRODUCTION

NAFLD refers to the accumulation of fat, mainly triglycerides, in hepatocytes leading to increase of the liver weight upto 5%, provided patient is taking less than 20 grams of alcohol/day (ie approximately 2 standard drinks), there is no alcohol abuse & no viral hepatitis[1]. NAFLD is now included as a component of metabolic syndrome[2]. Primary NAFLD results from insulin resistance & thus frequently occurs as part of the metabolic changes in obesity, dyslipidemia & T2DM[3]. Obesity has been reported in more than 40%, T2DM in more than 20% & hypertriglyceridemia in more than 20% persons having NAFLD. Secondary NAFLD is caused by a number of factors[4], including soft drinks consumption & cholecystectomy[2,5] more common in Hispanics than Asians2. If not adressed simple steatosis may progress to nonalcoholic steatohepatitis (NASH) leading to cirrhosis liver & thus hepatocellular carcinoma[6]. When de novo fatty acid synthesis or rate of hepatic fatty acid uptake from plasma is greater than the rate of fatty acid oxidation & export, steatosis develops[7]. Obesity, T2DM & older age are main risk factors for increased hepatic fibrosis & cirrhosis. Coffee consumption has been observed to reduce the rate of progression. Persons having NAFLD are at higher risk to get cardiovascular diseases, chronic kidney disease, & cancer of colorectal area[5]. Patients, both males & females, having NAFLD usually present in 4th to 6th decades. Patients may have other features of metabolic syndrome[8]. For confirmation of diagnosis, percutaneous liver biopsy is the gold standard but it is invasive, costly, may be associated with complications[9,10], to be done to exclude cirrhosis & hepatocellular carcinoma[11] & is generally not recommended in asymptomatic persons[5]. Macrovesicular steatosis may be demonstrated on ultrasonography, CT, or MRI, but not the steatohepatitis or fibrosis[5]. Ultrasound is the most commonly used imaging modality for the diagnosis of NAFLD, as it is cost effective, noninvassive, can be repeated to assess progression, in population based studies & has sensitivity of 80% & specificity of 99%10. We can grade the ultrasonographic features of NAFLD[12,13]. If the fat content in the liver falls below 30% then the sensitivity of ultrasound falls[2]. Another study reported sensitivity of ultrasound & CT scan to be 100% & 93% respectively[14]. Park SH et al concluded that if

Dr Saleem Iqbal (Corresponding Author)
Associate Professor Medicine, Medical B Unit, Khyber Teaching Hospital, Peshawar - Pakistan
Cell: +92-3339125084
Email: drsalimiqbal1@gmail.com

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the steatosis is more than 30% than CT scan has 100% specificity & 82% sensitivity[15], but can't be used for follow-up purposes, owing to radiations. MRI provides an accurate & rapid assessment of hepatic steatosis upto even a level of 3% & shows a good correlation with histological picture with sensitivity & specificity of 100% & 92.3%, respectively[16]. Proton magnetic resonance spectroscopy (MRS) even measures the fat proton fraction & hepatic triglyceride levels[2]. Fibroscan, is a noninvasive painless method that evaluates liver stiffness using pulse-echo ultrasound, but in obese people because of technical reasons its sensitivity is reduced[2]. Laboratory findings may be normal in up to 80% of persons with hepatic steatosis[5], however, serum aminotransferase & alkaline phosphatase levels may be mildly elevated. The ratio of ALT to AST is almost always greater than 1 in NAFLD[2]. NAFLD cannot be managed without treatment of underlying risk factors & lifestyle modification. A number of medicines have proved to modify risk factor profiles rather than as primary therapy for NAFLD[17]. Bariatric surgery (gastroplasty, Roux-en-Y gastric bypass (RYGB), & laproscopic gastric banding) is indicated in patients with body mass index greater 35 kg/m^2. Liver transplantation is now the 3rd most common (& most rapidly increasing) indication for advanced cirrhosis caused by NASH, in United States[5].

The prevalence of NAFLD is increasing worldwide. It has been recognized as the most common liver disease in USA where 20 to 45% of general populaton[2], 16-20 % of non obese individuals & 76-100% of obese & morbidly obese individuals[9] have already developed NAFLD. The situation is not different in Japan where 29% of healthy Japanese adults are currently having NAFLD[18]. The prevalence of patients having NAFLD is rapidly increasing not only in our general population, but also in our patients attending outpatient department, just like in the rest of the world. If left untreated, these patients may develop its complications. Thus to find out the frequency of patients having NAFLD in our General Medical OPD, we embarked on this study, for proper documentation and future referral.

MATERIAL AND METHODOS

After approval from the ethical committee, this observational study was conducted in General Medical Outpatient Department of Khyber Teaching Hospital Peshawar, from 4th April, 2017 to 3rd July, 2017. A total 436 patients who had NAFLD, as suggested on ultrasound, were included in the study after taking proper informed consent. Once a patient was reported to have NAFLD on ultrasound, in order to eliminate inter observer difference in opinion, the ultrasound was repeated by a radiologist having FCPS in diagnostic radiology, using Toshiba Xarto-100, 1.5 MHz probe. Patients with history of alcohol abuse, paediatric age group (less than 13 years), & patients with positive HBV & HCV serology, were excluded. Once the patients were diagnosed to have NAFLD, other investigations eg serum gamma GT, serum alkaline phosphatase, serum aspartate aminotransferase (AST), serum alanine amino transferase (ALT), Hepatitis B surface antigen & Anti hepatitis C virus antibodies, were done. T2DM was diagnosed on the basis of random plasma glucose, HbA1c & fasting plasma glucose (normal <126 mg%, a cut off value for diabetes mellitus). Proper fasting lipid profile, ECG & chest X-Rays were also done in all patients. The data was collected through a specially designed proforma. Frequencies & percentages were calculated for categorical variables. All the variables were presented in tables. Though MRI is better investigation than ultrasound & liver biopsy is gold standard, but our study was conducted in the outpatient department, most of the patients were not prepared for MRI liver & liver biopsy, so these were our limitations.

RESULTS

Out of 436 patients having NAFLD, only 74 patients i.e. 16.97% were males while females were 362 accounting for 83.02%, so male to female ratio was roughly 01 to 06, (Table 1). Majority of the patients ie 61.46% were in the age range 40-60 years, (Table 2). As the Table 3. Shows only 14 patients ie 3.21% had normal BMI while 80.49% patients were obese (BMI greater then 30). Type 2 Diabetes Mellitus was present in 28.37% males & 37.29% females as shown in Table 4. Serum cholesterol was elevated in 22.97% males & 20.16% females as shown in Table 5. Serum ALT was more than upper limit of normal in 54.05% males & in 38.39% females as shown in Table 6.

Table 1: Total patients seen in OPD & percentage of patients having NAFLD

Gender	Total Patients seen in OPD	Patients with NAFLD	Percentage having NAFLD
Females	1305	362	27%
Males	0702	074	10.54%
Total	2007	436	21.72%

DISCUSSION

We examined 2007 patients in general Medical outpatient Depatment, out of whom 436 patients ie 21.72% were found to have NAFLD. A similar study showed that 32% of patients had NAFLD in general

Table 2: Agewise percentages of patients having NAFLD

S. No	Age in years	Number	Percentage
1.	14-20	04	00.91%
2.	21-30	35	08.02%
3.	31-40	66	15.13 %
4.	41-50	114	26.14 %
5.	51-60	154	35.32 %
6.	61-70	54	12.38 %
7.	71-80	09	02.06%

Table 3: Degree of obesity of patients

S. No	Obesity	(BMI)	Number	Percentage
1.	Normal	18-24.99	14	03.21 %
2.	overweight	25-29.9	71	16.28 %
3.	class I	30-34.9	195	44.72 %
4.	Class II	35-39.9	91	20.87 %
5.	Class III	>40	65	14.90 %

Table 4: Status of T2DM in patients

S. No	Gender	Yes	No	Percentage
1.	Males	21	053	28.37 %
2.	Females	135	227	37.29%
	Total	156	280	35.77 %

Table 5: Status of serum cholestrol in patients

S. No	Gender	High (>200mg%)	Normal (<200mg%)	%age with hypercholesterolemia
1.	Males	17	57	22.97%
2.	Females	73	289	20.16%
	Total	90	346	20.64%

Table 6: Status of serum ALT in our patients (Normal values are <30iu/L for males & <19iu/L for females)

S. No	Gender	High	Normal	Percentage having high serum ALT
1.	Males	40	034	54.05%
2.	Females	139	223	38.39%
Total		179	257	41.05 %

Table 7: Showing status of serum AST in patients females)

S. No	Gender	High	Normal	Percentage high AST
1.	Males	02	072	2.70%
2.	Females	09	353	2.48%
Total		11	425	2.52%

medical OPD in a hospital based study conducted in India[10]. Though both the India & Pakistan are neighbour countries, & culture wise people of both the countries are almost similar, but there is quite significant statistical difference in percentage of people having NAFLD. Amongst the patients having NAFLD, 16.97% were males & 83.02% were females. A similar study done about a year ago, in the same area showed that 21.78% males & 78.21% females had NAFLD[17]. These figures are quite close to each other. While Targher G et al have reported NAFLD in 68% females[19]. NAFLD is more common in elderly post menopausal ladies20 & the ladies who use hormone replacement therapy have lesser chance of development of NAFLD[2]. In our study 83.02% patients were females & mostly were post menupausal in the age range 40-60 years, further the trend of HRT is not common in our population, so the percentage of ladies was significantly higher in our study. The prevalence of NAFLD increases with age, as Table 3 shows that 00.91% patient of age limit 14-20 years but 61.46% patients of 40-60 years had NAFLD. In the same age range a local study reported NAFLD in 59.21%[17] & another international study, NAFLD was reported in 65.4% patients of age limit 40–59 years[19]. All these three figures are very close to each other, thus supporting each other. NAFLD increases with the degree of obesity, Table 5 shows only 03.21 % patients with NAFLD had normal BMI, 16.28 % were over weight while 80.49% patients were obese in our study, which is very close to the figure of 78.21% in a local study[17] done a year ago. The figures presented by other studies are also very close to our figure eg NAFLD has been reported in 76-100% of obese (BMI>30 kg/m2) & morbid (BMI>35 kg/m2) obese persons[9], in 65–75% & 85–90% respectively in obese & morbidly obese individuals[21] & 24.5%, 67% & 94% in people with normal BMI, over weight & obese people respectively[22].

Type 2 Diabetes Mellitus was present in 28.37% males & in 37.29% females of our patients. 10-75% of NAFLD patients have been reported to have T2DM & 21-72% of patients with T2DM have NAFLD[4], while another local study has reported T2DM in 30.77% males & 35% females had NAFLD[17]. Association between obesity, steatosis & T2DM has already been recognized. Insulin resistance increases in people having hepatic steatosis & thus leading to T2DM[2]. T2DM speeds up liver fibrosis irrespective of other MS factors[5] & thus patients with liver disease having NAFLD & T2DM have greater risk of developing cirrhosis & thus higher mortality[2]. The commonest cause of elevated liver enzymes is NAFLD indicating hepatic steatosis, inflammation or fibrosis. However liver enzymes do not rise more than four times the upper limit of normal[23]. Serum ALT was elevated in 54.05% males and 38.39% females,collectively in both sexes s ALT was raised in 41.05%. These figures are slightly lower than the figures presented by another study[17], in which serum ALT was raised in 64.10% males, 50.71% females & collectively in both sexes serum ALT was raised in 53.63% of patients. These figures are also lower than the figure reported by Cortrim et al ie 65% collectively in both sexes[24] & similar observations have been published by Leite et al[25]. Serum AST level was elevated in only 2.52% of patients with NAFLD, Table 08, this figure is again closely correlating with the figure of 2.23% in an other study[17]. The ratio of serum AST to ALT is less than 1 in patients with simple steatosis, as the disease progresses the ratio is reversed[2].

CONCLUSIONS

NAFLD was more common in females, increases with age & was positively correlated with degree of obesity. T2DM, hypertension, ischemic heart diseases, dyslipedemias, & impaired liver biochemical tests results were more common in patients having NAFLD.

RECOMMENDATIONS

Patients having NAFLD are at increased risk of developing cardiovascular diseases, chronic renal diseases & carcinoma of colon & rectum. If left unadressed it may lead to NASH, liver fibrosis, cirrhosis & hepatocellular carcinoma. So there is a need of the hour that we should increase awareness about this rapidly increasing problem in our health care providers & general population to modify their lifestyle to prevent this increasing problem.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Iqbal S: Main Idea, Data Collection.

Khan S: Data Collection.

Iqbal MD: manuscript writting.

Iman NU: Overall supervision.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.