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Original Article

Frequency of Non-Alcoholic Fatty Liver Disease in Adults with Diabetes Mellitus

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ABSTRACT

Objective: To compare the frequency of non-alcoholic fatty liver disease in patients with diabetes of different age groups, body mass indexes and duration of diabetes.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Department of General Medicine, Combined Military Hospital, Quetta Pakistan, from Jun to Nov 2019.

Methodology: One hundred thirty-two patients of either gender with diabetes for more than one year were included. All patients underwent ultrasound to scan for fatty liver, and a consultant radiologist confirmed the findings. Non-alcoholic fatty liver disease was diagnosed as per operational definition.

Results: Of the total 132, 89(67.5%) were males, and 43(32.5%) were females. The mean age of the patients was 49.34±5.76 years. The mean weight of the patients was 72.91±13.40 Kg, the mean height was 1.56±0.09 meters, and 6.35±2.99 years was the mean duration of diabetes. Most patients were 46-60 years (78.8%). NAFLD was seen in 58.5% of patients with diabetes with female preponderance.

Conclusion: Non-alcoholic fatty liver disease was found to be more frequent in patients of the age group 46-60 years, and also it has a strong correlation with body mass index of >25 kg/m2 and longer duration of diabetes. A significant proportion of patients with diabetes were also found to have 'lean non-alcoholic fatty liver disease.

Keywords: Diabetes mellitus, Lean non-alcoholic fatty liver disease, Non-lean non-alcoholic fatty liver disease.

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INTRODUCTION

The rise in non-alcoholic fatty liver disease worldwide is quite similar to the prevalence rate of type-2 diabetes in many Countries (10%), with an estimated 382 million cases of diabetes across the globe and an exponentially growing trend in the upcoming two decades.[1] It has been reported in the literature that up to 70% of diagnosed patients with diabetes may have non-alcoholic fatty liver disease, while in asymptomatic type-2 diabetes (normal liver function tests), the prevalence of liver-biopsy proven Non-Alcoholic steatohepatitis was 20%.[2,3] In the United States, NAFLD is the commonest aetiology leading to chronic liver disease.[4]

The major contributing factor towards the burden of non-alcoholic fatty liver disease is secondary hepatic fibrosis in 5-7% of patients.[5] The latest development in the past decade has found that the disease burden is not limited to hepatic morbidity and mortality but is an emerging cause of extra-hepatic organs and regulatory pathway damage.[6] NAFLD increases the incidence of associated extra-hepatic chronic diseases like Diabetes Mellitus (type-2) and cardiovascular diseases by approximately two-fold, and the overall mortality rate secondary to NAFLD is up to 57%.[7,8]

Increased visceral adiposity (obesity) is frequently associated with NAFLD and other metabolic abnormalities, including dyslipidemias, increased insulin resistance, atherosclerotic changes and hypertension. Recent studies now regard NAFLD as a liver manifestation of metabolic syndrome as 80% of NASH patients were found to have increased BMI, dyslipidemias in 72% of patients and type-2 diabetes in 44% of cases. However, it is still under investigation whether diabetes is a risk factor for NAFLD or vice-versa.[9,10] Our objective was to compare the frequency of non-alcoholic fatty liver disease in diabetic patients of different age groups, body mass indexes, and duration of diabetes.

METHODOLOGY

The comparative cross-sectional study was conducted at the Department of General Medicine, Combined Military Hospital, Quetta Pakistan, from June to November 2019. The Hospital Ethical Review Committee approved the study protocol (CMH Qta

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IRB#009). The Sample size was calculated by using OpenEpi Software and considering a reference prevalence of 8%.[11]

Inclusion Criteria: Adult patients aged 30-60 years of either gender and patients with diabetes as per operational definition diagnosed for more than a year were included in this study.

Exclusion Criteria: Patients with diabetes secondary to hemochromatosis, chronic pancreatitis, drug or Cushing's syndrome, patients with chronic liver disease, cirrhosis secondary to viral or autoimmune hepatitis, excessive alcohol consumption greater than 30 g per day for males and 20 g for females, End-Stage Renal Disease (on maintenance hemodialysis) and obesity with BMI >30 were excluded.

The study included one hundred thirty-two patients who fulfilled the inclusion criteria from the Outdoor Patient Department of General Medicine. Demographic information of all patients [age, parity, BMI (BMI was calculated for each patient using the formula: weight on weighing machine (in kilogram) divided by height on height scale in a standing position (in meters) squared) and the total duration of diabetes] was recorded. Informed written consent was taken from participants, ensuring their confidentiality.[12] All patients underwent an ultrasound to scan for fatty liver, and a consultant radiologist confirmed the findings. A single author on self-made proforma noted data regarding NAFLD.

Statistical Package for Social Sciences (SPSS) version 25.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square test was applied to explore the inferential statistics. The *p*-value lower than or up to 0.05 was considered as

RESULTS

Of the total 132, 89(67.5%) were males, and 43 (32.5%) were females. The mean age of the patients was 49.34±5.76 years and ranges from 30-60 years. The mean weight of the patients was 72.91±13.40 Kg, the mean height was 1.56±0.09 meters, and 6.35±2.99 years was the mean duration of diabetes. Most patients were 46-60 years (78.8%). NAFLD was more frequent in female diabetic patients (65.1%). Non-alcoholic Fatty Liver Disease was seen in 55.3% of patients (Table).

Table: Association Non-Alcoholic Fatty Liver Disease with different Parameters (n=132)

Parameters	Non-Alcoholic Fatty Liver Disease		*p*-value
	Yes	No	
Age Groups (years)			
30-45	14(50%)	14(50%)	0.52%
46-60	59(56.7%)	45(43.3%)	
Gender			
Male	45(50.6%)	44(49.4%)	0.115
Female	28(65.1%)	15(34.9%)	
BMI			
≤25kg/m²	16(51.6%)	15(48.4%)	0.64
>25kg/m²	57(56.4%)	44(43.6%)	
Duration of Diabetes (years)			
2-5	14(21.2%)	52(78.8%)	0.001
>5	59(89.4%)	7(10.6%)	

DISCUSSION

We conducted this study to examine the frequency of Non-alcoholic fatty liver in clinically diagnosed patients with diabetes. In addition, we found a relationship between age, duration of clinically diagnosed diabetes and body mass index. In our Hospital of Pakistan, situated in the province of Balochistan, we have found NAFLD in 58.5% of diagnosed patients with diabetes by ultrasonography abdomen. The results of the frequency of NAFLD are also relatable to the results of other studies conducted in the region. Alavi *et al*. reported similar statistics from Lahore-Pakistan that 69% of patients with diabetes in his study had NAFLD.[11] Afzal *et al*. in a private hospital in Lahore, reported the same frequency of NAFLD in patients with type-2 diabetes as we discovered in our study. In his study sample, 53% of males and 61% of diabetic females had non-alcoholic fatty liver disease.[12] Luxmi *et al*. in their study at Karachi, showed a prevalence of 60.8% in Patients with diabetes.[13] All of them have used ultrasound abdomen as a diagnostic modality for hepatic steatosis. Zubair R *et al*. at Karachi, found the incidence of fatty liver to be 40% but showed almost similar frequency in both genders.[14] Gupte *et al*. from India, reported the occurrence of fatty liver to be 49% in patients with diabetes.[16]

The communities with a rising prevalence of obesity show quite a similar rising trend for NAFLD. A provocative study suggested that based on the trends of obesity in the US population will leave all US adults to be obese by 2048.[17] Marchesini *et al*. in their review, concluded that NAFLD has a very strong association with >25 kg/m² Body Mass Index, and it is supported by evidence that being overweight or obese is one of the risk factors for developing hepatic steatosis.[18] Our study found that 56.4% of overweight or obese (BMI>25) patients with diabetes had NAFLD. The

other striking finding was that 51.6% of normal-weight patients had 'lean NAFLD' (i.e. the diabetic patients with BMI <25 having NAFLD). A recent US study taking national data published one of the largest available data on 'lean NAFLD' so far and reported an overall prevalence of lean NAFLD to e 9.67%, while it was 28.8% for non-leans.[19] Dela Cruz *et al*. in their large prospective study of 11 years, found out that 'lean NAFLD' has severe outcomes in terms of prognosis. Leans with a fatty liver have shown severe lobular inflammation on hepatic histology, and they also have significantly higher mortality than non-leans (with NAFLD).[20]

Diabetes and NAFLD may act in synergy to result in the worst outcomes. An individual with NAFLD has a 5-fold risk of developing diabetes in a lifetime, and NAFLD is now considered an established risk factor for diabetes. Due to the insidious onset and disease progression of diabetes, it is less established and less evident that either diabetes has a positive association with the development of the fatty liver.[20] In our study, we have found a significant correlation between the duration of diabetes and hepatic steatosis, as 89.4% of those patients with diabetes who had clinically diagnosed diabetes for over five years had non-alcoholic fatty liver disease.

CONCLUSION

Non-alcoholic fatty liver disease was found to be frequent in patients of age group 46-60 years, and also it has a strong correlation with a longer duration of diabetes and body mass index of >25 kg/m^2. A significant proportion of patients with diabetes were also found to have 'lean non-alcoholic fatty liver disease.

Conflict of Interest: None.

Author's Contribution

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

RAY: & RUD: Conception, data acquisition, data analysis, data interpretation, approval of the final version to be published.

TAK: & AH: Study design, drafting the manuscript, critical review, approval of the final version to be published.

AMT: & MA: Critical review, data acquisition, drafting the manuscript, approval of the final version to be published.

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.

REFERENCES

1. International diabetes federation. IDF diabetes atlas: Executive Summary. Available at: <https://wwwidforg/sites/default/files/EN_6E_Atlas_Exec_Sum[Accessed on June 12, 2019]
2. Portillo-Sanchez P, Bril F, Maximos M. High prevalence of nonalcoholic fatty liver disease in patients with type 2 diabetes mellitus and normal plasma aminotransferase levels. J Clin Endocrinol Metab 2015; 100(6): 2231–2238. https://doi.org/ 10.1210/jc.2015-1966
3. Loomba R, Sanyal AJ. The global NAFLD epidemic. nat rev Gastroenterol Hepatol 2013; 10(11): 686-690. https://doi.org/10.1038/nrgastro.2013.171
4. Mishra P, Younossi ZM. Abdominal ultrasound for diagnosis of nonalcoholic fatty liver disease (NAFLD). Am J Gastroenterol 2007; 102(12): 2716-2717. https://doi.org/10.1111/j.1572-0241. 2007.01520.x
5. Szczepaniak LS, Nurenberg P, Leonard D, Browning JD, Reingold JS, Grundy S, et al. Magnetic resonance spectroscopy to measure hepatic triglyceride content: prevalence of hepatic steatosis in the general population. Am J Physiol Endocrinol Metab 2005; 288(2): E462-468. https://doi.org/10.1152/ajpendo.00064.2004
6. Armstrong MJ, Hazlehurst JM, Parker R. Severe asymptomatic non-alcoholic fatty liver disease in routine diabetes care; a multi-disciplinary team approach to diagnosis and management. QJM 2014; 107(1): 33–41. https://doi.org/10.1093%2Fqjmed%2Fhct198
7. Armstrong MJ, Adams LA, Canbay A, Syn WK. Extrahepatic complications of nonalcoholic fatty liver disease. Hepatology 2014; 59(3): 1174-1197. https://doi.org/10.1002/hep.26717
8. Musso G, Gambino R, Cassader M, Pagano G. Meta-analysis: natural history of non-alcoholic fatty liver disease (NAFLD) and diagnostic accuracy of noninvasive tests for liver disease severity. Ann Med 2011; 43(8): 617-649. https://doi: 10.3109/ 07853890.2010.518623.
9. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M, et al. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and out-comes. Hepatology 2016; 64(1): 73-84. https://doi:10.1002/ hep.28431.
10. Li Q, Dhyani M, Grajo JR, Sirlin C, Samir AE. Current status of imaging in nonalcoholic fatty liver disease. World J Hepatol 2018; 10(8): 530–542. https://doi:10.4254/wjh.v10.i8.530.
11. Alavi N, Amin S, Mumtaz M. Non-alcoholic fatty liver disease (NAFLD); frequency in diabetes mellitus (type ii) patients and non-diabetic group at Shalamar Medical and Dental College, Lahore. Professional Med J 2016; 23(1): 029-033. https://doi: 10.17957/TPMJ/16.3110
12. Afzal M , Anjum HS, Siddiqui UN and Shahid S. Nonalcoholic Fatty Liver Disease (NAFLD) Frequency in Diabetes Mellitus (DM) Type – II Patients. FUUAST J Biol 2016: 6(1): p7-p10.
13. Luxmi S, Sattar RA, Ara J. Association of non-alcoholic fatty liver with type 2 diabetes mellitus. Liaquat Uni Med Health Sci 2008; 18(3): 188-193.
14. Zubair R, Mirza M, Iftikhar J, Saeed N. Frequency of incidental fatty liver on ultrasound and its association with diabetes mellitus and hypertension. Pak J Med Sci 2018; 34(5): 1137-1141. https://doi.org/10.12669/pjms.345.15102
15. Akbar D, Kawther A. Nonalcoholic fatty liver disease in saudi type 2 diabetic subjects attending a medical outpatient clinic: Prevalence and genera characteristics. Diabetes Care 2003; 26(12): 3351-3352. https://doi.org/10.2337/diacare.26.12.3351-a
16. Gupte P, Amarapurkar D, Agal S, Baijal R, Kulshrestha P, Pramanik S et al. Non-alcoholic steatohepatitis in type 2 diabetes mellitus. J Gastroenterol Hepatol 2004; 19(8): 854-858. https:// doi.org/10.1111/j.1440-1746.2004.03312.x
17. Wang Y, Beydoun MA, Liang L, Caballero B, Kumanyika SK. Will all Americans become overweight or obese? Estimating the progression and cost of the US obesity epidemic. Obesity (Silver Spring) 2008; 16(10): 2323–2330. https://doi.org/10.1038/oby.2008.351
18. Marchesini G, Mazzotti A. NAFLD incidence and remission: Only a matter of weight gain and weight loss? J Hepatol 2015: 62(1): 15–17. https://doi.org/10.1016/j.jhep.2014.10.023
19. Younossi ZM, Stepanova M, Negro F, Hallaji S, Younossi Y, Lam B, et al. Nonalcoholic fatty liver disease in lean individuals in the United States. Medicine (Baltimore) 2012; 91(6): 319–327. https://doi.org/10.1097/md.0b013e3182779d49
20. Dela Cruz AC, Bugianesi E, George J, Day CP, Liaquat H, Charatcharoenwitthaya P, et al. Characteristics and long-term prognosis of lean patients with non-alcoholic fatty liver disease. Gastroenterology 2014; 146(6): S-909. http://dx.doi.org/10.1016/S0016-5085(14)63307-2