



Original Research Article

TO ASSESS CARDIO-VASCULAR RISKS IN DIABETES MELLITUS TYPE-2 AND ITS CORRELATION WITH NON ALCOHOLIC FATTY LIVER DISEASE

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Abstract: DM is the most common endocrine disease of human characterized by metabolic abnormalities leading to long term complication involving heart, kidney, liver, GIT, nerves and blood vessels, thereby causing morbidity and mortality. Diabetic patients often develop cardiovascular disease and it is the main cause of the high risk of premature death in these patients. Compared with non-diabetic subjects, people with tpe-2 DM appear to have an increased risk of developing Non-alcoholic fatty liver disease and certainly have a higher risk of developing fibrosis and cirrhosis. Metabolic syndrome is a strong predictor of Non-alcoholic fatty liver disease. A total number of 100 diabetic patients were included in the study. After the detailed history, clinical examination, ultrasonography and other planned investigations, 50 patients were found to have Non-alcoholic fatty liver disease while 50 patients were without Non-alcoholic fatty liver disease. The prevalence of metabolic syndrome in diabetic patients was 59%. 70% of Non-alcoholic fatty liver disease patients were having metabolic syndrome while in patients without Non-alcoholic fatty liver disease were having 48%. Metabolic syndrome is a well- known precursor of cardiovascular disease. Recognition of their presence, early diagnosis and management of these cardiovascular risk can reduce morbidity and mortality in diabetic patient.

Key Words: Diabetes Mellitus, Non Alcoholic Fatty Liver, Metabolic Syndrome, Cardiovascular risk.

INTRODUCTION

Diabetes is a chronic disease, which is reaching an epidemic proportion in many parts of world. Type-2 DM accounts for more than 90% of diabetic population worldwide. Both genetic and environmental factors are important in the development of the disease. Cardiovascular disease is increased in individuals with type-2 DM. The Framingham Heart Study revealed a marked increase in Coronary artery disease, Congestive heart failure, Myocardial infarction, Peripheral artery disease, and sudden death (risk increase from 1-5 fold) in DM. In addition to Coronary artery disease, cerebrovascular disease is increased in individual with DM (threefold increase in stroke). Non-alcoholic fatty liver disease (NAFLD), the liver manifestation of the metabolic syndrome, is now considered to be the commonest liver problem in the western world affecting 20-40% of the general population and also in other part of the world diagnostic criteria for diabetes.

- Symptoms of diabetes plus random blood glucose concentration >11.1 mmol/L (200 mg/dL)
- Random: without regard to time since last meal
Or
- Fasting plasma glucose level >7.0 mmol/L (126 mg/dL)
- Fasting: no caloric intake for at least 8 hours
Or
- 2-hour plasma glucose level >11.1 mmol/L (200 mg/dL) during oral glucose tolerance test
Or
- A1C ≥ 6.5%*

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Type 2-diabetes mellitus is a progressive chronic disease with long-term complications causing high associated morbidity and a considerable economic and social burden.¹⁻³ Diabetic patients often develop cardiovascular disease and it is the main cause of the high risk of premature death in these patients.⁴⁻⁷

1. Coronary artery disease (CAD): Indians have 3 times higher risk of developing CAD compared to Chinese and are 20 times more likely to die due to CAD compared to native black or white South Africans⁸⁻⁹
2. Diabetic retinopathy: In India with epidemic increase in DM Diabetic Retinopathy is fast becoming a burden leading to morbidity among the earning age group
3. Diabetic Nephropathy: DN is the leading cause of ESRD (End stage renal disease) worldwide¹⁰
4. Others: PVD(Peripheral vascular disease) prevalence in Indians is lower than that reported in western studies

Cardiovascular Morbidity and Mortality¹¹

Cardiovascular disease is increased in individuals with type 1 or type 2 DM. The Framingham Heart Study revealed a marked increase in PAD, CHF, CAD, MI, and sudden death (risk increase from one- to fivefold) in DM. The American Heart Association has designated DM as a major risk factor for cardiovascular disease (same category as smoking, hypertension, and hyperlipidemia)



Non-alcoholic fatty liver disease

This study is to assess whether NAFLD is independently related to cardiovascular disease. Non-alcoholic fatty liver disease (NAFLD), the liver manifestation of the metabolic syndrome, is now considered to be the commonest liver problem in the western world affecting 20-40% of the general population and also in other parts of the world. NAFLD is a common clinical condition with histological features that resemble those of alcohol-induced liver injury, but occur in patients who do not abuse alcohol. NAFLD encompasses a histological spectrum ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), advanced fibrosis, cirrhosis, liver failure, and hepatocellular carcinoma (HCC).

MATERIAL AND METHODS

The study was conducted in the Department of Medicine, Guru Nanak Dev hospital, Amritsar, Punjab. The study included 100 patients who were admitted from July 2012 to Oct 2014. The patients involved in the study are included according to the exclusion and inclusion criteria.

Inclusion criteria

- All patient known case of type –2 DM
- All patient taking specific medication for diabetes
- All patient having fasting blood sugar > 126 mg/dl attending OPD or admitted in wards
- Patient giving consent for the study

Exclusion criteria

- Subjects taking alcohol or with alcohol consumption > 20 g/day
- Subjects with other known causes of chronic liver disease
 - Viral hepatitis (HbsAg + ve, Anti HCV +ve)
 - Autoimmune hepatitis
 - Use of hepatotoxic medications
 - Glucocorticoids
 - Antibiotics
 - Amiodarone
 - Tamoxifen
 - Antineoplastic drugs

Metabolic syndrome diagnosed according to ATP-III 2001 definition ≥ 3 of the following.

1. Central obesity – Waist circumference > 102 cm. in male and > 88 cm in female.
2. Triglyceride ≥ 150 mg. / dl.
3. HDL < 40 mg /dl. in male and <50 mg/dl. in female
4. Hypertension BP systolic ≥ 130 mmHg or diastolic ≥ 85 mmHg or patient is taking any specific treatment for hypertension.

5. Fasting plasma glucose ≥ 100 mg/dl. Or specific medication or previously diagnosed type - 2 DM.

Hepatic USG scanning performed by experienced radiologist who were blinded to subject details. The diagnosis of hepatic steatosis were made on the basis of characteristic sonographic features:

1. Increased echogenicity of liver
2. Increased liver contrast compared to kidney.
3. Vascular blurring – mainly of hepatic veins.
4. Attenuation of echogenic level in deep seated area.

USG has a sensitivity of 90% and specificity of 95% in detection of moderate and severe hepatic steatosis.

RESULT

- A total number of 100 diabetic patients were included in the study. After the detailed history, clinical examination, ultrasonography and other planned investigations, 50 patients were found to have NAFLD while 50 patients were without NAFLD. Group A and Group B respectively.
- Most diabetic patients were female (52%) with mean age is 59 yr.
- The prevalence of NAFLD in diabetic patients was 50% and with advancing age its prevalence increases.
- 52% of patients with NAFLD were having diabetes for 5 or more than 5 years of duration.
- 82% of NAFLD patients were associated with higher serum ALT level i.e. >19U/L in women and >30U/L in men (p value <0.05 statistically significant).
- The prevalence of metabolic syndrome in diabetic patients was 59%.
- 70% of NAFLD patients were having metabolic syndrome while in patients without NAFLD were having 48% (p value <0.001 statistically significant).
- 60% of NAFLD patients were having BMI ≥ 25 kg/m² which was statistically significant.
- Majority of NAFLD patients having triglyceride level on higher side.
- Most common cardiovascular complication found in the study sample was hypertension (54%) followed by CAD (50%), PVD (14%), and CVA (11%).
- Hypertension (52%), CAD (56%) and CVA (18%) were found in patient of NAFLD
- The burden of cardiovascular complication was high in patients of NAFLD in comparison to the patients of without NAFLD.
- 19% of hypertensive was newly diagnosed during the study.

Table 1: showing alt level in both groups

ALT LEVEL (U/L)	GROUP-A (no.=50)	GROUP-B (no.=50)
Normal	9	20
Abnormal	41	30

Majority of cases with NAFLD were having higher ALT level i.e. 82% (41), whereas in group B 60% (30) patients were having higher SGPT level which was statistically significant (p value < 0.05).

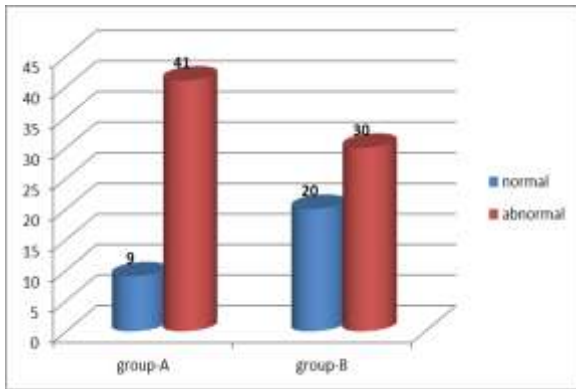


Table 2: Showing metabolic syndrome (ms) distribution in both groups

MS IN	GROUP-A (50)	GROUP-B (50)	TOTAL NO CASES
MALE	16	13	29
FEMALE	19	11	30
TOTAL	35	24	59

Prevalence of Metabolic syndrome in diabetic patients were 59% and in group A and group B were 70% and 48% (p value < 0.001).

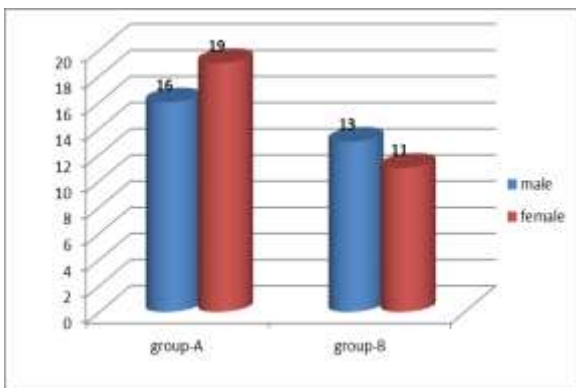


Table 3: showing triglyceride level in both the groups

TGL LEVEL(mg/dl)	GROUP-A (50)	GROUP-B (50)
<150	23	44
≥150	27	6

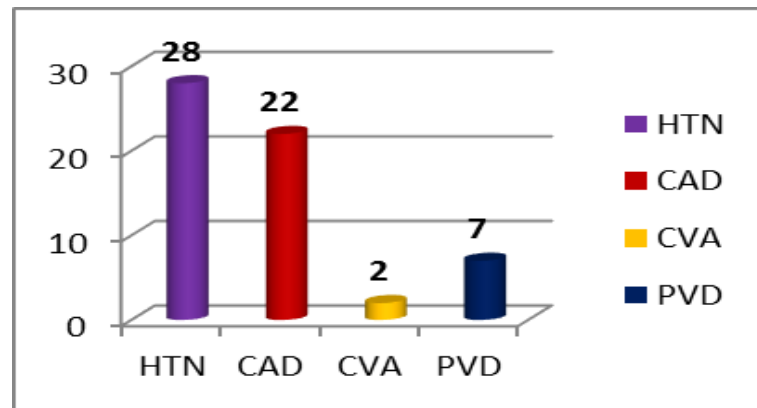
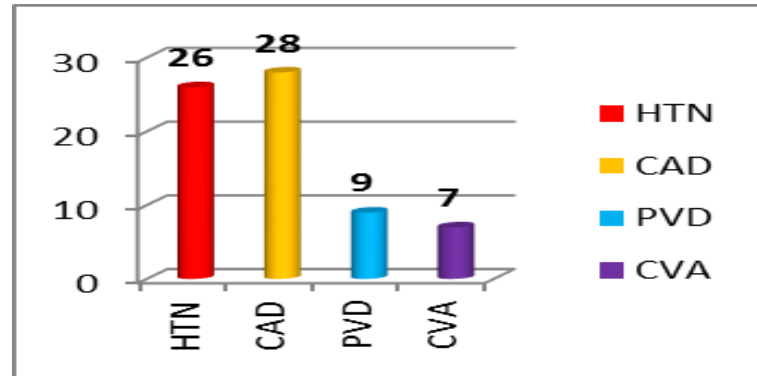
IF TGL LEVEL CUT OFF

<140	14	43
≥140	36	7

In Group A 54% of the patient were having TG >150. In group B 12% of patient were having TG >150. In group A number of patient increased from 27 to 36 on decreasing the cutoff level of TGL to 140 mg/dl

Table 4: Prevalence of CVD in both groups

CARDIOVASCULAR COMPLICATION	GROUP-A (50)		GROUP-B (50)	
	No.	%	No.	%
HYPERTENSION	26	52	28	56
CAD	28	56	22	44
CVA	9	18	2	4
PVD(ABI <0.9)	7	14	7	14



DISCUSSION

Type-2 DM is characterized by an increased risk of CVD in men and women. In particular, there is an excess prevalence of CAD in diabetic patient. Non-alcoholic fatty liver disease is increasingly recognized as a public health problem in medical community. The pathogenesis of NAFLD is multifactorial. A lot of experimental and clinical data point to NAFLD as a hepatic expression of the metabolic syndrome¹². Because of the underlying metabolic disorder, NAFLD patients are expected to have higher risk of vascular and coronary heart disease. The potential cardiovascular risk of NAFLD¹³⁻²³ itself has not been investigated. 100 diabetic patients who were admitted in medicine wards, were screened and out of these 100 individual fulfilled the criteria for inclusion. Of these 100 individual, 50 had hepatic steatosis on USG and remaining 50 patients had normal sonography of liver.

In this study out of 100 included patients 48 were males. But in most of the studies it was reported that there is equal prevalence of diabetes in both the

sex. In the present study prevalence of diabetic were more in females.

In the present study, majority of cases in both the genders were in the age group 40-60 yrs. In the present study, the prevalence of NAFLD found in diabetic were 50%. The prevalence of NAFLD increased with increasing age (27% cases among age group 40-50 yrs and 40% among those aged 51-60 yrs).

In the present study, patient with NAFLD were older and more likely to be female same as without NAFLD. As expected, majority of individuals with NAFLD had longer duration of diabetes than those without NAFLD. In the study, 52% of patients with NAFLD were having diabetes for duration of 5 or more than 5 yrs whereas patients without NAFLD 42% were having the same duration. Patient of NAFLD also had higher values of liver enzyme i.e. ALT level. When more stringent criteria were used in our study (i.e. ALT > 30 U/L in men and > 19 U/L in women)¹³⁷, 82% of NAFLD patients were having higher ALT level while in group B 60% of patients were having higher ALT level which were statistically significant ($p < 0.05$).

We used the criteria of NCEP ATP III for characterize the metabolic syndrome. We had taken BMI of $\geq 25 \text{ kg/m}^2$ for all patients as an index of obesity in place of waist measurement. A BMI of $\geq 25 \text{ kg/m}^2$ has been proposed as a cut-off for the diagnosis of obesity in Asian people. Individuals with 3 or more of the 5 abnormalities were considered to have metabolic syndrome. Metabolic syndrome and its individual component occurred more frequently among NAFLD. In the present study 59% diabetic patients were having metabolic syndrome. A limited amount of data exist on the prevalence of metabolic syndrome in India.

In the present, 70% of NAFLD patients were having metabolic syndrome while individual without NAFLD were having only 48%. As it is already reported in literature that NAFLD is the hepatic manifestation of metabolic syndrome so it well support our present findings. On analyzing individual component of metabolic syndrome, it was found that 60% of group A were having BMI $\geq 25 \text{ kg/m}^2$ and in case of group B patients only 48% having BMI $\geq 25 \text{ kg/m}^2$ ($p \text{ value} < 0.05$ which is statistically significant).

In the present study, majority of group B individual having blood pressure on higher side. 62% of group B patient were having systolic BP $\geq 130 \text{ mmHg}$ and 54% were having diastolic pressure $\geq 85 \text{ mmHg}$. As we know that hypertension is common finding in diabetic patients and it has been reported that the chances of hypertension increases in patient of NAFLD

having diabetes. But our study does not correlate with this finding.

In the present study, NAFLD was more common in individuals who had higher triglyceride level ($\geq 150 \text{ mg/dl}$) as compared to those individuals without NAFLD. On taking lower cutoff level of triglyceride as abnormal ($\geq 140 \text{ mg/dl}$) for metabolic syndrome the proportion of NAFLD patients with abnormal triglyceride level was increased to a significant level in comparison to non NAFLD patients ($p > 0.001$). It suggest that the chances of NAFLD will be more even if the criteria for abnormal triglyceride level is decreased to 140 mg/dl.

In our study, 36% patients of NAFLD was having abnormal HDL level in comparison to 18% in patients without NAFLD suggesting more chances of NAFLD with abnormal level of HDL in diabetic patients. Type-2 DM is a progressive chronic disease with long term complication causing high associated morbidity and considerable economic and social burden. Diabetic patients often develop cardiovascular disease and it is the main cause of the high risk premature death in these patients. The problem of NAFLD is not confined to its potential to cause serious liver related morbidity and mortality. NAFLD frequently occurs with features of metabolic syndrome and metabolic syndrome is a well-known precursor of CVD. Many studies are done to know the prevalence of CVD in diabetic patients having NAFLD.

In the present study the prevalence of coronary, cerebrovascular and peripheral vascular disease were higher in males than females. In this study, CVD was higher in NAFLD patients as compared to patients not having NAFLD. 52% of patients were having hypertension and 56% were having CAD in comparison to patients without NAFLD having 56% hypertension and 44% CAD. The other views is that in India, due to poor socioeconomic status, diabetes diagnosed very late and patient often present with cardiovascular complications.

In the present study, 18% of patients with NAFLD were having CVA while 4% cases of CVA was found in patient without NAFLD. There are more chances of CVA in diabetic patients having NAFLD. We have also found 14% of NAFLD patients having PVD while 14% patients without NAFLD. During the analysis of all 100 diabetic patients, CAD was found in 50 patients out of whom 28 patients were having NAFLD and 22 patients were without NAFLD. These patients with CAD were further evaluated to know the distribution of NAFLD with CVD and metabolic syndrome. The distribution of CVD in CAD patients were: 22.4%- AWWMI, 28.57%- IWMI, 14.2%- Ischemia,

28.5%-Angina, 51.02%- hypertension (30.61%-old and 20.4%-newly diagnosed), and 8.16%- CVA. Except for AAMI which was high in patients without NAFLD, both groups were comparable. But in CAD patients, metabolic syndrome and its individual components occurred more frequently among patient with NAFLD in comparison to non NAFLD patients.

CONCLUSION

In the present study it is concluded that the prevalence of NAFLD in diabetic patients was 50%. It was also observed that prevalence of CVD was higher in NAFLD patients as compared to the patients without NAFLD. It implies that NAFLD is independent and added risk factors for CVD in patients of type 2 DM. Recognition of their presence, early diagnosis and management of these cardiovascular risk can reduce morbidity and mortality in diabetic patient.

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