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PREVALENCE OF PREDIABETES AND TYPE-2 DIABETES MELLITUS WITH HEPATITIS C VIRUS INFECTION

Medicine

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KEYWORDS:

INTRODUCTION:

Type 2 diabetes mellitus (T2DM) and HCV (hepatitis C virus) infection are the important public health problem. There is marked geographic variation exists for HCV infection rates ranging from 1.3%-1.6% in the United States to 15% in Egypt(1). The population prevalence of HCV infection is 1% and of T2DM is 8.3% in India(2). HCV-related cirrhosis is the leading indication for liver transplantation in the western world.(3) Chronic hepatitis C virus infection mainly affects liver but can be associated with various extrahepatic manifestations including arthritis, vasculitis, sicca syndrome, porphyria cutanea tarda, lichen planus, nephropathies, lung fibrosis and B-cell lymphoproliferative diseases.(4) Chronic hepatitis C (CHC) is further associated with endocrinal disorder namely T2DM, metabolic syndrome, and atherosclerosis.(5) A large number of studies report an increased risk of T2DM in patients with chronic hepatitis C virus infection(6)(7). HCV and its association with T2DM were first confirmed in HCV-related cirrhosis by Allison et al(8). Subsequent studies had confirmed that such association was present in every stage of HCV infection.(9,10) whereas few studies could not confirm this association in the absence of liver dysfunction(6). Association of CHC and T2DM holds true even when comparing patients with HCV related liver disease compared to that of HBV related liver disease(11,12).

MATERIALS AND METHODS:

Study Design: A cross-sectional study was conducted on 100 HCV seropositive patients attending Guru Nanak Dev Hospital, Amritsar, Punjab, India.

Inclusion criteria: Newly diagnosed or previously known HCV positive patients aged between 18 and 75 years.

Exclusion criteria: History of alcohol abuse, known (familial) hyperlipidemia, known case of T2DM, co-infection with hepatitis B virus infection or HIV infection, and hepatocellular carcinoma.

A standard questionnaire was used which included a detailed history and examinations. All the study subjects were then subjected to Anti-HCV (ELISA method), RBS, FBS, two-hour plasma sugar, HbA1C, liver function test and ultrasound of abdomen. T2DM and prediabetes were diagnosed based on standard ADA criteria.(13) Metabolic syndrome was diagnosed based on Harmonizing definition.(14)

Statistics: For the purpose of making comparisons the study population was divided into three groups which are non-diabetic group(Non-DM), prediabetic(Pre-DM) group and diabetic(DM) group. Systematically collected and compiled data was statistically analyzed using IBM SPSS 22.0 software to draw cross-tabs and make relevant conclusions. The data was expressed as means, standard deviation, number and percentages. One way ANOVA and x2-test (Chi-square test) was applied to calculate p values. The p value of <0.05 was considered as significant, p-value of <0.001 as highly significant and p-value of >0.05 was considered as non-significant.

RESULT:

Among the HCV seropositive study subjects, the prevalence of T2DM was 36% whereas the prevalence of prediabetes was 39%.

Metabolic syndrome was present in 69.4% of DM subjects, 64.1% of pre-DM subjects and 32% of Non-DM subjects. Metabolic syndrome was significantly more common in the pre-DM and DM group compared to non-DM group.(P=0.009).

Out of 100 study subjects, 52 were indoor subjects and 48 were outdoor subjects. Amongst the total of 48 outdoor subjects, 33% (16/48) were non-diabetic, 44% (21/48) were having prediabetes and 23% (11/48) were having T2DM. Amongst the total of 52 indoor subjects, only 17% (9/52) were non-diabetic, whereas 34% (18/52) were having prediabetes and 48% (25/52) were having T2DM (p=0.0085).

TABLES AND FIGURES:

FIGURE 1. PREVALENCE OF T2DM AND PREDIABETES IN THE STUDY POPULATION

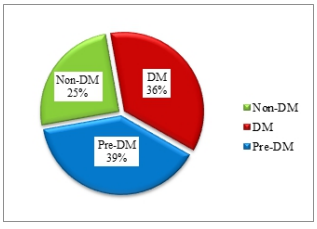

TABLE 1. STUDY RESULT IN FORM OF MEAN, STAND DEVIATION AND P-VALUE WITH COMPARISON OF VARIOUS PARAMETERS INTO THREE STUDY GROUPS

	Non-DM	Pre-DM	DM	p-value
n (F/M)	25(13/12)	39(28/11)	36(26/10)	-
Age (years)	44.16±15.09	41.49±13.36	44.92±15.31	0.568
BMI(kg/m2)	24.11 ± 1.71	25.82 ± 2.89	27.28 ± 2.37	<0.001
RBS(mg/dl)	114.52±23.69	129.41±38.18	215.31±89.14	<0.001
FBS(mg/dl)	88.88±6.83	104.28±13.45	172.03±54.92	<0.001
Two-hr plasma sugar (mg/dl)	119.28±12.94	162.28±21.40	241.36±56.68	<0.001
HbA1C(%)	5.02±0.47	6.14±0.16	7.48±0.80	<0.001
S. Cholesterol(mg/dl)	146.80±32.24	156.41±32.04	179.08±38.66	0.001

S. Triglyseride(mg/dl)	126.44±30.76	143.90±50.81	166.31±44.78	0.003
HDL (mg/dl)	43.80±6.37	39.71±6.95	42.50±5.43	0.030
LDL (mg/dl)	77.71±31.44	87.92±27.70	103.32±35.17	0.007
VLDL(mg/dl)	25.29±6.154	28.78±10.164	33.26±8.956	0.003
HTN	13/25(52%)	17/39(43.6%)	18/36(50%)	0.770
USG: -Fatty liver -Cirrhosis liver	5/25(20%) 5/25(20%)	11/39(28.2%) 10/39(25.6%)	11/36(30.6%) 10/36(27.8%)	0.644 0.783

HTN: hypertension; BMI: body mass index; RBS: random blood sugar; FBS: fasting blood sugar; HDL: high density lipoprotein; LDL: low density lipoprotein; VLDL : very low density lipoprotein;

DISCUSSION:

The prevalence of T2DM was 36% in the present study, which was signifiantly higher as compared to the population prevalence of T2DM in India which is 9.1%.(15) Fraser GM et al observed slightly higher prevalence of T2DM in subjects with HCV-related liver disease, i.e 39.1% (16) while Lecube et al obsereved 32% prevalence of T2DM in subjects with HCV-related liver disease (17). Zein NN et al, Mason et al and Howard AA et al found the prevalence of T2DM in subjects with HCV related liver disease to be 25%, 21% and 15% respectively, showing a positive association between chronic HCV infection and T2DM.

The prevalence of prediabetes was 39% in the present study, which was higher than the normal population. Desouky DE et al and Ali AA et al found the prevalence of prediabetes to be 63.8% and 64% respectively, which is much higher than the prevalence of our study. The reason behind this difference might be the difference in the study population, as cirrhosis liver was excluded in their study.(20,21) The present study concluded that 75% of HCV seropositive patients presenting to the tertiary care hospital in Punjab have a glycemic abnormality in the form of either prediabetes or T2DM.

Insulin resistance has been found to be the major pathologic mechanism by which HCV alters glucose homeostasis, leading to prediabetes or T2DM. Insulin resistance in chronic hepatitis C develops due to impairment in insulin signaling in hepatocyte(22), oxidative stress to hepatocytes(23) and hepatic steatosis(24). Insulin resistance can also induce steatosis, so HCV-related steatosis and insulin resistance are interrelated. Increased inflammatory mediators and cytokines are also associated with insulin resistance(25).

Development of T2DM was found to be independent of age in our study whereas multivariate analysis by Mason et al. revealed that age was independent predictors of T2DM(11). This variation in result was attributable to the small study population.

In the present study, 67% of HCV seropostive individuals were male and the rest, i.e 33% were females , which is in accordance with a similar study done by Singh P et al in this (Punjab) region of India, where 72.87% were males and 27.13% were females.(26) One possible explanation for this may be the fact that males are more prone to harbor the risk factors for HCV infection, like injectible drug users as compared to females.

T2DM and prediabetes were more common in males compared to females but the difference was not statistically significant. A study was by Caronia et al also showed increased risk for development of NIDDM in males (27), whereas a study done by Ryu et al showed no significant gender difference among HCV-seropositive patients for development of T2DM.(28) Data of various studies are inconclusive of any role of gender in relation to the development of T2DM in CHC subjects.

Prevalence of T2DM was significantly more common in indoor admitted subjects whereas the prevalence of prediabetes was significantly more common in outdoor subjects compared to indoor subjects (p=0.0085).

BMI was found to be one of the risk factors for the development of T2DM in HCV-seropositive cases in the present study. Mehta et al and Wang et al have also concluded BMI to be an important risk factor. (10) (29)

Patients with CHC also demonstrated reduced levels of circulating LDL and total cholesterol, compared to healthy controls.(30) But our study showed the contradictory result as cholesterol, triglyceride and LDL level increases with the development of prediabetes and T2DM compared to non-diabetic subjects.

In the present study, the difference in the development of glycemic abnormality in patients with fatty liver and cirrhosis was not statistically different. Many evidences support this link as HCV is able to induce insulin resistance independent of steatosis or fibrosis.(31) This conclusion is comparable to the result of a study done by Knobler H et al in which they concluded that increase in the prevalence of T2DM was independent of cirrhosis of the liver.(9)

The overall prevalence of HTN was 48% in the present study i.e. comparable to 41.6% in the study by Butt et al(32).

Prevalence of metabolic syndrome increased in HCV-seropositive cases with prediabetes and T2DM as compared to non-diabetic patients in the present study. In a study done by Oliveira LPM et al, the prevalence of metabolic syndrome was 21.6% in HCV-seropositive patients which is significantly lower compared to our study. Such difference might be related to different study population as patients with BMI > 30 kg/m2 were excluded from their study.(33)

There are certain limitations of this study. The most important limitations in this study are small sample size, single centered tertiary care hospital based study and cross-sectional design. The large-scale, prospective and population-based study is required to determine the prevalence of T2DM accurately.

CONCLUSION :

The prevalence of T2DM was significantly increased in HCV-seropositive patients compared to the population prevalence of T2DM. 75% of the study population had a glycemic abnormality in form of prediabetes or T2DM. BMI had significantly increased T2DM and prediabetes subjects compared to non-diabetic subjects. Prevalence of prediabetes and T2DM was not increased with age. The gender difference was not associated with the development of T2DM. Subjects with T2DM were having significantly high cholesterol, triglyceride, LDL, and VLDL level. Development of glycemic abnormality was independent of cirrhosis or fatty liver.

ETHICS:

The approval of institutional thesis and ethical committee was granted before initiating. The study subjects were informed about the study procedure and written informed consent was taken.

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