

Original article:

A study of Prevalence of Hepatitis C in type 2 Diabetes Mellitus in Central Rajasthan

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Abstract

Back ground: Hepatitis C virus (HCV) infection and diabetes mellitus (DM) are two major public health problems, we try to find out prevalence of HCV in DM

Objectives: To find the prevalence rate of HCV infection in patients with Type 2 DM in Central Rajasthan

Methods: Cross-sectional study was conducted in the Department of Medicine, JLN medical college and Associated hospital, Ajmer (Raj), on the patient including 400 Type 2 DM patients and 100 non-diabetic person was screened for Hepatitis C.

Results: Out of 400 diabetics, 38 [9.5%] were found to be HCV positive while among non diabetics only 3 [3.0%] were found HCV positive. ($p < 0.05$) The HCV positivity was highest in male and in the lower socioeconomic class

Conclusion: HCV positivity higher among diabetes than non diabetes and co-existence of these two conditions is more than coincidental.

Keywords: HCV, DM

Introduction

The incidence of diabetes has been increasing steadily. In Asia, 3–10% of the general adult population suffers from type 2 diabetes. It is therefore not surprising to find a large number of individuals suffering from both chronic hepatitis C and diabetes. [1] Hepatitis C virus (HCV) infection and diabetes mellitus (DM) are two major public health problems that cause devastating health and financial burdens worldwide. Chronic hepatitis C virus (HCV) has become the global "epidemic" with an estimated 123 million people currently infected worldwide. At the same time diabetes is also rapidly emerging as a global health care problem that threatens to reach pandemic levels by 2030. [2] Chronic hepatitis C and type 2 diabetes mellitus are common conditions.

Around 160 million people worldwide are estimated to be chronically infected with hepatitis C virus (HCV). In many countries, HCV has surpassed HIV as the leading viral cause of mortality. [3]

Hepatitis C Virus

The link between the HCV and diabetes was first reported by Allison et al. in 1994 and later explored by Simo and colleagues in 1996. The initial idea that patients with T2DM have more parenteral exposures because of use of finger stick devices and thus are at an increased risk of contacting blood borne infections such as HCV was disproved by a study from France in 1998.

The epidemiological link between T2DM and HCV has been investigated from two perspectives. Various studies have shown high HCV seropositivity

among patients with T2DM as compared to the control group, prevalence being two to seven times higher in the diabetic group. However, other investigators performing did not find such an association of HCV with T2DM. In addition, several studies have shown that HCV increases the risk of development of T2DM. The mechanism of pathogenesis of diabetes in patients with HCV infection remains unclear though it has been implicated that insulin resistance plays an important role and is related to fibrosis score. Although there is a growing body of literature on the link between T2DM and HCV, the studies are contradictory and the data is inconclusive and it is not known if diabetes is a risk factor for the development of HCV. [6]

Outcome in diabetic HCV-Positive patients

CHC is an insidiously progressive form of liver disease that leads to cirrhosis and HCC. Diabetic HCV-positive patients have increased risk compared with non-diabetic subjects, and DM itself seems to have a selective impact on HCC development.

The main characteristic of diabetic patients is IR, which plays a crucial role in fibrosis progression and has a negative impact on treatment responses to antiviral therapy in patients with CHC. Reduced insulin sensitivity is at the basis of compensatory hyperinsulinemia and elevated levels of insulin-like growth factor 1 (IGF-1), which stimulates cell proliferation and inhibits apoptosis. Additionally, this phenomenon has strong mitogenic effects on a wide variety of cancer cell lines. [4]

At the same time, insulin activates the IGF-1 receptor, which has a growth-promoting effect that includes modulating cell cycle progression. Excess insulin may also indirectly affect the development of cancer by down regulating the level of IGF-binding protein 1, which increases the level and bioavailability

of total circulating IGF-1. Genotype differences in terms of liver disturbance progression have been described as well. Genotype 3a is more strongly correlated with steatosis than other genotypes, and the HCV genotype 3 may have a cytopathic effect. Steatosis in genotype 1 infection is instead thought to be an expression of metabolic syndrome caused by the activation of proinflammatory mechanisms as well as underlying obesity and IR. [3] Many epidemiological studies have shown an association between T2DM and CHC. The processes through which HCV is associated with DM seem to involve direct viral effects, IR, proinflammatory cytokines, chemokines, suppressors of cytokine signalling, and other immunemediated mechanisms.

Many epidemiological studies have demonstrated the significant association between T2DM and chronic HCV infection. [6] Insulin resistance (IR) and type 2 diabetes mellitus (T2DM) are serious extrahepatic manifestations of chronic hepatitis C virus (HCV) infection. However, the mechanism underlying the IR in chronic HCV is obscure. Hepatokines are a group of liver-derived proteins, which affect the glucose and lipid metabolism in several tissues. Fetuin A (also known as human α 2-HS-glycoprotein) is one of the hepatokines, which was recognized as a natural inhibitor of the insulin receptor tyrosine kinase in liver and skeletal muscle. Additionally, selenoprotein P has emerged as an important hepatokine, which primarily acts as a selenium transporter and has been reported to be implicated in glucose homeostasis in human.

Chronic hepatitis C is a systemic disease inducing metabolic alterations leading to extrahepatic consequences. In particular, hepatitis C virus (HCV) infection seems to increase the risk of incident type 2 diabetes mellitus in predisposed individuals,

independently of liver disease stage. Many studies have reported the clinical consequences of type 2 diabetes mellitus on hepatitis C outcome, but very few studies have addressed the issue of microangiopathic complications among patients with hepatitis C only, who develop type 2 diabetes mellitus. [5]

Moreover, clinical trials in HCV-positive patients have reported improvement in glucose metabolism after antiviral treatment; recent studies have suggested that this metabolic amelioration might have a clinical impact on type 2 diabetes mellitus-related complications. These observations raise the question as to whether the HCV eradication may also have an impact on the future morbidity and mortality due to type 2 diabetes mellitus. Whether HCV infection is the cause of diabetes or diabetic patients are more prone to get HCV infection is still in question. [1]

Aims and objects

To find the prevalence rate of HCV infection in patients with Type 2 DM.

Material and methods

The present Cross-sectional study was conducted in the Department of Medicine, JLN medical college and Associated hospital, Ajmer (Raj), after having obtained permission from the Institutional ethical committee and written informed consent of the patient including 400 Type 2 DM patients and 100 non-diabetic person was screened.

Study population: All known cases of Type 2 DM who fulfilled the inclusion criterion during the study period.

Inclusion criterion:

1. All known cases of Type 2 DM
The criteria for diagnosis of diabetes (ADA guidelines, 2011):

- a) Fasting plasma glucose ≥ 126 mg/dl.
Fasting is defined as no calorie intake for at least 8 hours.
- b) HbA_{1c} $\geq 6.5\%$.
- c) 2 hour plasma glucose ≥ 200 mg/dl during an Oral glucose tolerance test.
- d) In a patient with classic symptoms of hyperglycaemia or hyperglycaemic crisis, a random plasma glucose ≥ 200 mg/dl.

Exclusion criterion:

1. Patients with liver failure, malignancy, IV drug user, risky sexual behavior, alcohol use, blood transfusion or any other chronic illness.

Methods:

1. All the patients were taken a voluntary consent before the start of the study. No patient was forced to participate in the study.
2. Socio-demographic variables like age, sex, address, religion, race, etc was used.
3. The patients was subjected to investigations which includes:
 - a) Random blood sugar.
 - b) Blood glucose fasting and post prandial (whenever required).
 - c) Liver function test.
 - d) HCV antibody screening.
 - e) HbA_{1c}
 - f) Lipid profile.
4. Then the data of each patient was recorded, tabulated and descriptive statistic like percentage and proportion and appropriate significance test was used for analysis.

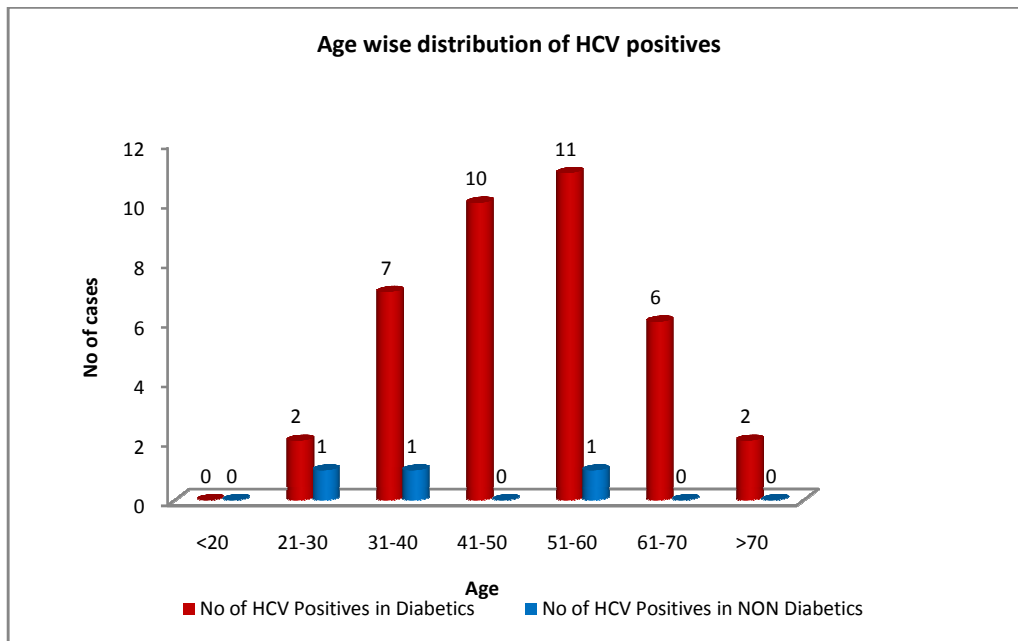
Results

Tab 1. HCV positivity in Diabetics and controls

Participants	No of cases	No of HCV Positives	% HCV Positive
Diabetics	400	38	9.5
Non Diabetics	100	3	3.0
Total	500	41	8.2

Table 2. Age wise distribution of participants and HCV positivity

Age in years	No of Diabetics	No of NON Diabetics	No of HCV Positives in Diabetics	No of HCV Positives in NON Diabetics	% of HCV Positives in Diabetics	% of HCV Positives in NON Diabetics
<20	0	8	0	0	0.0	0.0
21-30	5	9	2	1	40.0	11.1
31-40	53	19	7	1	13.2	5.3
41-50	79	21	10	0	12.7	0.0
51-60	94	18	11	1	11.7	5.6
61-70	115	13	6	0	5.2	0.0
>70	54	12	2	0	3.7	0.0
Total	400	100	38	3	9.5	3.0



Tab 3. Sex wise distribution of participants and HCV positivity

SEX	No of Diabetics	No of NON Diabetics	No of HCV Positives in Diabetics	No of HCV Positives in NON Diabetics	% of HCV Positives in Diabetics	% of HCV Positives in NON Diabetics
Male	243	58	31	2	12.8	3.4
Female	157	42	7	1	4.5	2.4
Total	400	100	38	3	9.5	3.0

Discussion

In this study 500 participants were included, 400 [80%] were suffering from diabetes and as controls 100 [20%] non diabetics were included.

Solomon et al [7] conducted a case control study on a total of 604 study subjects, 304 subjects with diabetics and 300 non-diabetic controls. **Greca et al [8]** performed Serologic-HCV testing in 489 type 2 DM patients (303 outpatients and 186 on dialysis).

In the study of **Nauman et al [9]** the study population comprised of 3000 patients with diabetes and 10,000 controls recruited from the blood bank.

Saxena et al [10] retrospectively reviewed The records of 196 patients with ESRD , Of the 196 patients 54 (27.5%) had type-2 diabetes mellitus and 142 (72.5%) were non-diabetics.

HCV Positivity

In this study out of 400 diabetics, 38 [9.5%] were found to be HCV positive while among non diabetics only 3 [3.0%] were found HCV positive. This was statistically significant [p=0.034], chi square test applied.

Very much similar to our study **Solomon et al** found the prevalence of HCV in type II diabetes and non-diabetic controls was 9.9% and 3.3%, respectively.

Greca et al found HCV positivity (HCV+) was observed in 39 of 303 (12.9%) diabetics.

Nauman et al recorded a Prevalence rate of 13.7% for HCV infection among subjects having T2DM with seropositivity rate of 4.9% among the control

group of volunteer blood donors without diabetes ,They concluded that the patients with T2DM were more likely to have HCV infection as compared to the control group (OR = 3.03, 95%CI = 2.64-3.48, p = 0.001).

Saxena et al found the overall, HCV sero-prevalence of 41.3% (81/196) and annual seroconversion rate of 8.26%. Of the 196 patients 54 (27.5%) had type-2 diabetes mellitus and 142 (72.5%) were non-diabetics. Patients with type-2 diabetes recorded higher HCV prevalence (57.4% vs 35.2%).

Age

Among diabetics the age ranged from 28 to 75 years, the mean age was 59.4 ±7.9 years, however the age range of non diabetics was 19 to 72 years, the mean age was 48.7 ±8.6 years.

Among Diabetics the majority of the HCV positives were in 41-60 years of age group [21, 24.4%], followed by 31-40 years [7, 13.2 %]. But no such predilection was observed in non diabetics.

In the study of **Solomon et al** the result indicated that there was statistical significant difference in age between diabetic and non diabetic controls (17.456 years) (P = 0.000, and in the study of **Greca et al** Mean patient age was 60 years.

Nauman et al observed that the mean age of diabetes patients was 48.19 ±10.32 years and Majority of patients with T2DM were in the age group 36-45 years (34.7%). They also noted that the

Diabetic patients with age above 55 years had higher prevalence rate as compared to younger individuals

Sex

Among 400 diabetics majority were males [243, 60.75%] and 157 [39.25%] were females, While among non diabetics 58 [58.0%] were males and 42 [42.0%] were females.

Among male diabetics the HCV Positivity was 12.8 % [31/243] but in female diabetics it was lower 7/157 [4.5%] this difference was statistically significant [p=0.005]

In the study of **Solomon et al** of the diabetic subjects, 188 (61.8%) were males and the rest 116 (38.2%) were females. On the other hand, 170 (56.7%) males and 130 (43.3%) females were included from non-diabetic controls. The male to female ratio of diabetics and non diabetic controls was 1.62 and 1.3, respectively.

Greca et al found that among HCV+ patients, 32 were men (43.8%), Nauman et al observed that Majority of patients with T2DM were female (55.7%) however male patients had significantly high seropositivity as compared to female patients (15.3% vs. 12.4%, p = 0.02).

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Conclusions

1. Out of 400 diabetics, 38 [9.5%] were found to be HCV positive while among non diabetics only 3 [3.0%] were found HCV positive.
2. Among male diabetics the HCV Positivity was 12.8 % [31/243] but in female diabetics it was lower 7/157 [4.5%]
3. The HCV positivity was highest in the lower socioeconomic class 13/87 [14.9%], 18/186 [9.7%] in middle class and lowest 7/127 [5.5%] in upper class.
4. The HCV positivity was almost equal in all levels of BMI in Diabetic cases.
5. HCV positivity was higher among cases with longer duration of diabetes. It was 11 % in cases with > 5 years history and 9.8% in cases with 1-5 years history and only 4.4% in cases with <1 years history.
6. Among dyslipidemics 29 [9.3 %] were HCV positives while among normal lipid cases 9 [10.3%] were HCV positive.
7. Among diabetics of urban areas 25 [8.7 %] were HCV positives while among rural area cases 13 [11.5%] were HCV positive.

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