Original Article

FREQUENCY OF TYPE 2 DIABETES MELLITUS IN PATIENTS WITH CHRONIC HEPATITIS C VIRUS INFECTION

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ABSTRACT:

BACKGROUND: In developing countries, Diabetes Mellitus and Hepatitis C virus infection are major public health problems. A range of extra-hepatic manifestation such as artharlgia, thyroiditis and Type 2 Diabetes Mellitus are associated with Hepatitis C virus infection. Almost one-third of the patients suffering from Chronic Hepatitis C virus infection develop Type 2 Diabetes Mellitus.

OBJECTIVE: 1 To study the prevalence of Type 2 Diabetes Mellitus in Chronic Hepatitis C virus patients.

METHODOLOGY: A case-control study was conducted from June 2014 to Dec 2014 at Madinah Teaching Hospital. A non-probability convenient sampling technique was used, after approval from hospital ethical committee. Participants with evidence of chronic Hepatitis C virus infection, in form of positive ELISA, positive PCR for HCV RNA with raised serum ALT, were evaluated for presence of Type 2 Diabetes Mellitus. Clinical and ultrasonographic evidence of cirrhosis in these participants were also checked. These participants (cases) were then compared with healthy blood donors (controls) visiting blood donation centre in Madinah Teaching Hospital, for Hepatitis C virus infection and presence of Type 2 Diabetes Mellitus.

RESULTS: 242 participants suffering from Chronic Hepatitis C infection were inducted. Out of these 242, 53% (n= 128) were male and 47% (n= 114) were females, with male to female ratio 1.2: 1. Type 2 Diabetes Mellitus was present in 27% (n= 66) of the participants. Maximum number 75.5% (n= 183) diabetic patients were in age group of > 40 years. In our study genotype 3 was most prevalent, 83% (n= 201), followed by genotype 1, in 11% (n=27) of participants. Healthy donors were considered as control group. Out of these controls (n=242), only 3.3% (n= 8) were positive for Hepatitis C virus infection. In these 3% only one person was found to diabetic according to WHO criteria.

CONCLUSION: The prevalence of Diabetes Mellitus in patients with Chronic Hepatitis C infection is higher than in the general population. This prevalence is even higher in healthy blood donors with Hepatitis C, emphasizing that only presence of Hepatitis C virus is not sufficient to produce the Type 2 Diabetes Mellitus but it is the presence of Chronic Hepatitis C which is fundamental.

KEY WORDS: 1 Chronic Hepatitis C, 2 Diabetes Mellitus, 3 Cirrhosis, 4 Prevalence

INTRODUCTION:

Hepatitis C virus (HCV) infection is a frequent cause of acute and chronic hepatitis, and leads to the development of cirrhosis and hepatocellular carcinoma. It is estimated that about 150 to 200 million people have been in contact with HCV worldwide, and approximately 85% are chronically infected. The spectrum of severity of liver disease associated with HCV varies widely, as does the rate of progression towards the cirrhotic stage. The latter seems to depend on several, mostly host-related cofactors, such as age, sex, level of alcohol consumption, overweight, immune status and co-infections [1,2] One of these cofactors is type 2 diabetes, which has been recognized to modify the course of hepatitis C even at the stage of insulin resistance (IR), a condition that precedes the development of type 2 diabetes [3,4.] Although individuals may develop IR independently of HCV, a considerable amount of clinical and experimental data suggests that HCV contributes to its pathogenesis. Insulin resistance seems not only to accelerate the course of chronic hepatitis C, but also to influence the response to antiviral therapy[5.]The Chronic liver disease due to hepatitis C is greatest among developing countries, the highest reported prevalence are in China (3.2%) Egypt (22%) Pakistan (4.8%) [7]. Within Pakistan the HCV prevalence rate varies between the four provinces, prevalence rate reported in Punjab is 6.7%, in Sindh 5%, in Baluchistan 1.5% and in Khyber Pakhtunkhwa 1.1% [8]. High prevalence areas of HCV in Punjab are Vehari, Okara, Jhang, Islamabad, Attock, Rahim Yar Khan, Mandi Bhauddin, Gujranwala and Mianwali [8]. Globally, it is estimated that 382 million people worldwide have Diabetes Type 2 with a prevalence of 8.3%. In 2004, an estimated 3.4 million people died from the disease. WHO projects that Diabetes will be the 7th leading cause of death in 2030. Diabetes has become an important public health problem in Pakistan with 7.1 million diabetics in 2010 expected to rise to 13.8 million in 2030 when the country will rank fourth in terms of number of patients aged 20-79 with diabetes [9].High frequency of diabetes mellitus and hepatitis C in Pakistan led to initiation of this study.

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MATERIAL AND METHODS:

This study was conducted from June 2014 to Dec 2014 at Madinah Teaching Hospital using non probability convenient sampling technique. After approval from hospital ethical committee, a case-control study was conducted.

Inclusion Criteria:

Patients who were visiting Madinah teaching hospital with chronic hepatitis due to HCV, with raised ALT for more than 6 months, positive anti-HCV antibodies or positive PCR for HCV RNA were included. Cirrhosis of liver was confirmed by ultrasonography. Individuals who were having chronic hepatitis due to HCV with raised liver enzymes Initially but converted to normal after treatment with either Interferon or Ribavirin, were also included this study. These patients were either sex, admitted in ward (gastroenterology or hepatology) or were visiting medical OPD.

Exclusion Criteria:

Patients of chronic hepatitis and liver cirrhosis, of any known cause other than hepatitis C virus infection, were excluded from study. Patients with liver cancer, on interferon therapy, having end stage renal disease or coexisting viral infections like hepatitis B surface antigen positive patients and pregnant females were also excluded from the study.

Informed consent was taken from participants and data was collected on structured, pre-tested questionnaire.

242 controls were selected, who visited blood donation centre. These individuals were tested for their hepatitis c status based on raised liver enzymes for more than 6 months and cirrhosis of liver. HCV positive individuals were further tested for presence of diabetes mellitus.

Comparisons of frequencies of diabetes mellitus

of two groups (cases and controls) were done by measuring proportions.
Fasting blood samples of all the participants were taken at two consecutive days. Diabetes mellitus was labeled according to WHO criteria; those having fasting blood glucose level more than 126 mg/dl were considered diabetic.
Other laboratory investigation includes complete blood picture, serum cholesterol, serum albumin, total bilirubin, prothrombin time and serum creatinine levels.
Categorical variables were presented as frequencies and percentage. The prevalence of type 2 Diabetes Mellitus among hepatitis C seropositive was calculated and presented as percentage. Age was categorized into two groups (<40 years and >40 years). The dependent variables were age, weight, gender, family history of diabetes and HCV genotyping.

RESULTS:

A total of 242 subjects were included in the study. The mean age of the study participants was with a range 18 to 65 years. Male and females proportions were almost equal in our study sample, 53% and 47% respectively. Majority of the study population were married (93.5%) as compared to single ones (6.5%). Overall prevalence of type 2 diabetes mellitus among HCV sero-positive patients was 27%.

Frequency of cirrhosis in chronic hepatitis C patients (N=242)

	No of Patients	Percentage
Cirrhotic	87	35%
Non Cirrhotic	155	65%

Age distribution of chronic hepatitis C patients studied (N=242)

	No of Patients	Percentage
18 – 40	59	24.5%
> 40	183	75.5%

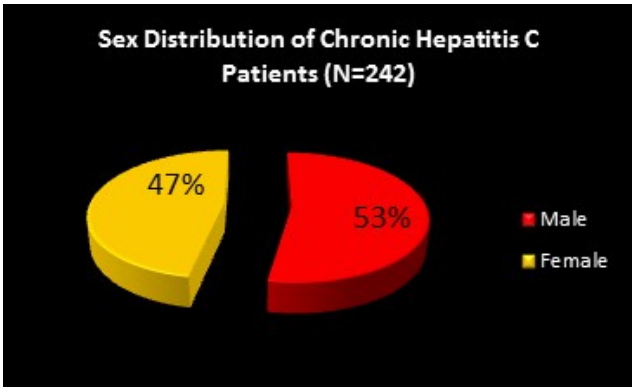
Frequency of Type 2 Diabetes Mellitus (T2DM) in chronic hepatitis C patients (N=242)

	No of Patients	Percentage
T2 DM	66	27%
Non-Diabetics	176	73%

Frequency of Genotype in chronic hepatitis C patients (N=242)

Viral Genotypes	No of Patients	Percentage
Genotype 1	27	11%
Genotype 2	04	1.5%
Genotype 3	201	83%
Genotype 4	10	4.5%

Sex Distribution of Chronic Hepatitis C Patients (N=242)



DISCUSSION:

Up to one third of patients with chronic hepatitis C virus (HCV) develop type 2 diabetes mellitus

(DM). This prevalence is much higher than that observed in the general population, and in patients with other chronic liver diseases such as hepatitis B virus, alcoholic liver disease, and primary biliary cirrhosis. [10]

In our study we observed prevalence of type 2 diabetes as 27%, out of 242 HCV seropositive patients. When we compare prevalence of type 2 diabetes in HCV seropositive patients as compared to controls we found twice higher rate of prevalence of type 2 diabetes in HCV seropositive patients. The first research that established the link between chronic hepatitis due to HCV and type 2 diabetes mellitus; was conducted by Allison et al [11]. According to their study type 2 Diabetes was 5 times more common in chronic hepatitis patients as compared to general population. In our study prevalence of type 2 diabetes mellitus was 27% which is similar to the study conducted in Jhelum by Shahid et al, where they found 26% prevalence [12]. Similar results were seen in another study conducted in Faisalabad by Dilshad et al; where they found 34.8% prevalence [13]. In contrast to this, low prevalence (18.7%) was observed in a study conducted in Rawalpindi- Islamabad by Khoker N [14]. Studies conducted in Japan and USA; the prevalence observed was 20.9% and 21% respectively [15,16]. This difference in various regions may be attributed to regional variation in prevalence of hepatitis C infection.

Data from the previous literature and from our study show a strong association between HCV and type 2 diabetes. Several reasons can explain the association of type 2 diabetes with HCV. One of the explanations is that the pathophysiology of HCV-associated type 2 diabetes mellitus consists of a defect in insulin secretion, increased hepatic tumor necrosis factor alpha, excessive hepatic glucose production, and insulin resistance, because the core-encoding region of HCV is sufficient to induce insulin resistance by the previously defined mechanism via either direct or indirect way [17].

In our study type 2 diabetes was more prevalent in chronic hepatitis patient whose age was >40 years as compared to younger age group (18-40 years). This finding is consistent with a study conducted in Mexico and United States [18,19].

In our study 35% of the seropositive patients had evidence of cirrhosis on clinical or on ultrasonography. Studies conducted in different parts of the world show similar results in which type 2 diabetes mellitus was more frequent in cirrhotic patients as compared to non-cirrhotic and it varied from 19.5% to 50% [20,21,22]. It can be concluded from this relationship that with advancing liver disease there will be increased susceptibility of HCV seropositive patients to develop type 2 diabetes mellitus.

We observed in our study that gender difference was not important factor in association of Chronic Hepatitis C and diabetes mellitus. Similar results were observed in another study conducted by Elhawary et al [23]. In contrast to this, a study conducted by Coronia et al. found that type 2 diabetes mellitus was more common in male patients [24]. This association found in our study and other study may not be ignored because type 2 diabetes is more common in males as compared to females in general population[25, 26]. So, this relationship should be evaluated in another study on larger scale.

The most common genotype was 3 in our study which was prevalent in 83% of the study population. In other studies conducted in Pakistan genotype 3 is most common [13, 27]. Controversies regarding the presence of a specific genotype in HCV seropositive diabetic patients are still a part of scientific debate, and larger scale studies are required to find a conclusion regarding which genotype is more specifically affecting diabetic HCV seropositive patients. However, our study observed that the HCV seropositive population with genotype 3 was significantly associated with type 2 diabetes mellitus.

In our study there was very low prevalence of type 2 diabetes mellitus in HCV positive healthy blood donors which were considered as controls. This low prevalence of diabetes mellitus in these HCV positive blood donors was probably due to the absence of chronic hepatitis as evident by normal serum ALT. This supports the already established fact that diabetes mellitus is more prevalent in those HCV positive individuals who have evidence of chronic hepatitis.

CONCLUSION:

The prevalence of type 2 diabetes mellitus is

more frequent in Hepatitis C patients as compared to general population. This has strong implications on early detection and treatment of Chronic Hepatitis C infection. As our study was hospital based so it is need of hour, to conduct population based, large sample studies to further evaluate this association.

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This world is not a permanent place, it is a passage, a road on which you are passing. There are two kinds of people here: One is the kind of those who have sold their souls for eternal damnation, the other is of those who have purchased their souls and freed them from damnation.

He is the wisest and the most knowing man who advises people not to lose hope and faith in the Mercy of Allah and not to be too sure and over-confident of immunity from His Wrath and Punishment.

Like your body your mind also gets tired so refresh it by wise sayings.

That knowledge which remains only on your tongue is very superficial. The intrinsic value of knowledge is that you act upon it.

Hazrat Ali (Karmulha Wajhay)