FREQUENCY AND COMMON RISK FACTORS LEADING TO HEPATITIS C VIRUS INFECTION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Objective: To determine the frequency of hepatitis C virus infection in patients with type 2 diabetes mellitus and to look for the common risk factors leading to this infection in diabetics.

Study Design: Descriptive cross sectional study design.

Place and Duration of Study: Department of Medicine, Combined Military Hospital (CMH) Kharian, from Jan 2015 to Jun 2015.

Patients and Methods: This study was conducted in the department of Medicine, Combined Military Hospital Kharian. Through a descriptive cross sectional study design, a total of 140 patients with type 2 diabetes mellitus, admitted through casualty, OPD or private clinics were selected and tested for Hepatitis C virus infection. The common risk factors leading to such infection among positive cases were also scrutinized.

Results: The mean age of patients was 48.82 ± 10.14 with 60.7% female gender predominating the overall sample of diabetics. Using 3rd generation ELISA method, hepatitis C virus was found in 45 (32.1%) of patients with 41-50 years of age group most commonly affected age group (34.7%) and female (57.8%) commonly affected gender. The distribution of risk factors leading to hepatitis C virus in diabetics are: 21 (46.7%) had history of surgery in the past, 13 (28.9%) had history of blood transfusion in the past, 7 (15.55%) had history of hemodialysis while only 4 (8.9%) had history of tattooing in the past.

Conclusion: Hepatitis C virus infection is still a common problem in diabetic patients of our local population and we recommend further research work over its risk factors so that the guidelines for its control may be formulated.

Keywords: Blood transfusion, Diabetes Mellitus, Haemodialysis, Hepatitis C virus infection, Risk Factors, Surgery, Tattooing.

INTRODUCTION

Hepatitis C virus (HCV) is one of the most common cause of chronic liver disease with fatal complications as the end stage of cirrhosis and liver cancer[1]. According to thelatest statistics, the prevalence of HCV infection is round about 3% and affects more than 170 million people globally[2]. Chronic hepatitis C virus infection mainly affects liver andit can be associated with various extrahepatic manifestations including; cryoglobulinemia, glomerulonephritis, sialadenitis and porphyria cutaneatarda[3,4].

Diabetes mellitus is a chronic endocrine disease that affects metabolism causing abnormal glucose homeostasis[5]. Worldwide more than 171 million people are affected by diabetes mellitus, and this figure is expected to rise up to 366 million by 2030[6]. Jayawardena *et al*. in their meta-analysis and systemic review showed burden of diabetes ranging from 3% to 7.2% in a general population of Pakistan[7]. When comparing with European individuals, type 2 diabetes mellitus is 4- to 6-fold more prevalentin South Asian[8].

HCV infection is mainly developed through a multi-factorial process and it is associated with various risk factors, as observed with all other infectious diseases. These are associated with the development of infection include virus-related factors (e.g., genotype and viral load) and host-related factors, such as age, gender, blood transfusion status, alcohol consumption, obesity, immune status, and co-infections factors. One of

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the important cofactor is type 2 diabetes mellitus. T2DM has been shown to modify the course of hepatitis C virus infection, even at the insulin resistance (IR) stage, which precedes the development of overt diabetes. It is now generally recognized that chronic hepatitis C is a metabolic disease that is strongly associated with T2DM and IR[8]. History of blood transfusion, tattoo, surgical procedures and haemodialysis are the common roots for contracting HCV infection.

This study was crucial in determining whether there was a need to screen persons with one of these common conditions for the other, given the adverse outcomes caused by each can be medically prevented. It has provided an evidence based conclusion for a policy to screen persons with type 2 diabetes mellitus for HCV and will help in creating awareness in diabetics about the more strict preventive measures for the common risk factors of HCV infection. Similarly early detection of hepatitis C virus infection in patients of diabetes mellitus can also lead to interventions with significant positive impact on disease progression and antiviral therapy outcomes.

PATIENTS AND METHODS

This is a descriptive cross sectional study carried out in department of Medicine, Combined Military Hospital, Kharian (Pakistan) between 1st January 2015 to 30th June 2015 after approval by the hospital ethical committee. All patients between the age group of 30–70 yearsof both the sexes were included in this study. Total of 140 patients with type 2 diabetes mellitus[8], admitted through casualty, OPD or private clinics were selected and tested for HCV infection, were included using "WHO Sample Size Calculator".

While the exclusion criteria were; patients with type 1 diabetes mellitus, previously diagnosed diabetes mellitus with HCV coinfection and intravenous drug abusers.

Written informed consent, demographic data and history was taken from the patients. Patients with fasting glucose ≥7mmol/L (126mg/dl) and random ≥11.1 mmol/L (200mg/dl) were consi-

dered diabetics. Venous blood was taken for fasting and random glucose levels and the detection of anti HCV antibodies by ELSIA 3rd generation machine which was performed by the biochemist and microbiologist respectively. All investigations were sent to hospital laboratory and the results were followed. In patients with positive Anti HCV Antibody, history about common risk factors for HCV infection like blood transfusion, any minor or major surgery, tattooing and haemodialysis even once in the past was taken.

Descriptive statistical data was analyzed by IBM (International Business Machine) SPSS version 17. In data analysis, mean ± standard deviation were calculated for quantitative variables like age, age at diagnosis of diabetes, duration of diabetes and frequency/percentages were calculated for categorical variables like gender, anti-Hepatitis C Virus antibody. Chi square test was used keeping p-value <0.05. All the results were presented as tables and graphs.

RESULTS

The study group comprised of 140 diagnosed cases of type 2 diabetes mellitus. All patients between the age group of 30-70 years of both the sexes with mean age of 48.82 ± 10.14. Majority of patients 75 (53.6%) were in the age range 41-50 years, followed by 33 (23.6%) patients in the age group 51-60 years, 20 patients (14.3%) in the age range 33 to 40 years and 12 patients (8.6%) were in the age range 60 + years (table-I).

Analysis showed that the patients with type 2 diabetes have significantly higher frequency of HCV infection. The distribution of HCV infection in diabetic patients was then studied with respect to age, gender, marital status and duration of diabetes.

Based on the duration of diabetes, study subjects were grouped into: >5-10 years with 43 (30.7%) of the sample, 11-15 years with 52 (37.2%) of the sample, while in the group with duration of diabetes of 15+ years we had 45 (32.1%) of the overall sample of 140 (table-II).

A total number of 140 patients who were confirmed type 2 diabetics were studied for the evidence of anti HCV antibodies. There were 85 (60.7%) females and 55 (39.3%) males with a female to male ratio of 1.5:1 (table-III).

Screening for the presence of anti HCV antibodies, were positive in 45 (32.1%) patients in the entire study group. Among the HCV positive patients while stratifying it among gender, 19

groups 41-50 years 26 (34.7%) were HCV positive, in the age group by 51 to 60 years 11 (33.33%) out of 33 were HCV positive, in the age group 60+ years out of total 12 patients 4 (33.33%) were HCV positive while in the age group 33-40 years out of total 20 patients, 4 (20%) were HCV positive (table-V).

Considering the duration of diabetes condi-tion amongsubjects recruited, in this study, it

Table-I: Age-wise distribution (n=140).

Age ranges (in years)	No. of cases	Percentage (%)
33-40	20	14.2
41-50	75	53.6
51-60	33	23.6
>60	12	8.6
Total	140	100

Table-II: Distribution of duration of diabetes (n=140).

Duration of Diabetes	No. of cases	Percentage (%)
>5-10	43	30.7
11-15	52	37.2
>15	45	32.1
Total	140	100

Table-III: Frequency of HCV infection in patients with type 2 diabetes (n=140).

Test	No of Patients	Percentage (%)
HCV Positive	45	32.1
HCV Negative	95	67.9
Total	140	100

Table-IV: Gender wise distribution of HCV positive patients (n=45).

Gender	No. of Patients	HCV Positive	Percentage (%)
Male	85	19	42.2
Female	55	26	57.8
Total	140	45	32.1

Table-V: Age-wise distribution of hcv positive patients (n=45).

Age ranges (in years)	No. of Cases	Percentage (%)
33-40	4	20
41-50	26	34.7
51-60	11	33.33
>60	4	33.33
Total	45	100

(42.2%) were males and 26 (57.8%) were females, showing high predilection for female gender (table-IV).

It was observed that older patients were more likely to have HCV infection as compared to those in the younger age groups which was evident when we did age wise stratification of the HCV positivity. Out of 75 patients in the age

became evident that as the duration of diabetes progresses, the frequency of HCV infection also increases. In the group of patients with duration of diabetes between 5-10 years out of total 43 patients[9] (20.9%) were HCV positive, in the group with duration of 10-15 years of total 52 patients 20 (38.5%) were HCV positive and in the group with duration of diabetes of more than 15 years

of total 45 patients 16 (35.6%) were HCV positive (table-II).

While looking into the risk factors which led to the acquisition of HCV infection, we considered four potential risk factors including history of blood transfusion, any (major/minor) surgical procedures, tattooing and haemodialysis in the past. In the analysis of risk factors we found that out of total 45 HCV positive diabetics, 21 (46.7%) had history of surgery in the past, 13 (28.9%) had history of blood transfusion in the past, 7 (15.55%) had history of haemodialysis while only 4 (8.9%) had history of tattooing in the past.

DISCUSSION

The liver is one of the vital organs involved in glucose metabolism, the others being skeletal muscle, brain and adipose tissue. A link between chronic liver disease (CLD) and type 2 diabetes mellitus was first observed by Allison *et al*. in 1994 and later explored by Simo and colleagues in 1996[9,10]. Different cross sectional studies have found a higher prevalence of HCV antibodies in type 2 diabetic patients than expected in the general population[11,13,14]. In addition, all studies in which a control group of non-diabetic subjects had been included found a significantly higher prevalence of HCV antibodies in type 2 diabetic patients[12-14].

Many different explanations have been suggested including autoimmunity, insulin resistance, cytokines, iron overload and direct beta cell dysfunction resulting from invasion by HCV virus[8,9]. The term hepatogenic diabetes has been rightly described for these patients having diabetes secondary to liver disease.

Our study shows a significant increase in HCV infection in diabetic patients. 32.1% of our diabetic patients turned out to have hepatitis C. This approximates to the previously reported studies where 27.6% occurrence had been reported from Bahawalpur and 31.25% by Khokhar[12], Ali *et al* in their studies conducted in Pakistan. Similarly, Bahtiyar *et al* found a higher prevalence of HCV seropositivity in diabetic patients

than in the general population in the United States of America. Furthermore, Knobler and Schattner found a positive association between HCV infection and type 2 diabetes mellitus among their Israeli patients. The studies conducted by Mason *et al*.[11] and Ryu *et al* working separately, supported a positive association between HCV infection and diabetes mellitus among American and Korean patients respectively.

Because age is an important risk factor for type 2 diabetes mellitus, we analyzed the relation of HCV infection and type 2 diabetes mellitus by stratified age Figure. The analysis showed that anti HCV positive participants in the age group 41 to 50, 51 to 60 and 60 + years had a higher chance of developing diabetes compared to other age groups. This fact has also been supported by a study from Taiwan. In our study, subjects between 33-40 years of age, recorded a significant prevalence of HCV infection, which contrasts with the report of Mehta *et al*.[11] that type 2 diabetes occurs more freqent with HCV infection in those older than 40 years of age.

However this age group is also at a greater risk of developing diabetes apart from coexisting HCV infection, so case control studies will be fruitful to assess this aspect in depth.

The decreased prevalence in T2D patients younger than 40 years of age would be consistent with the inference that HCV infection causes type 2 diabetes through progressive liver damage. This idea is supported as the liver is the principal organ in carbohydrate metabolism, the association of type 2 diabetes with other causes of cirrhosis, and evidence that liver transplantation can reverse both glucose intolerance and insulin resistance associated with diabetes. However, our study showed a high frequency of HCV infection in diabetic patients. As such we must have further studies in our younger population to identify the risk factors.

This analysis showed in relation to the duration of type 2 diabetes onset, that those who suffered from diabetes within the period of 10 years had a seroprevalence of 20.9% as compared

with those who had suffered from diabetes for longer duration. This reflects thelong term damage of the virus in the liver resulting in disturbed carbohydrate metabolism.

The younger the persons with HCV infection, the greater is the risk that they will develop diabetes than their similar counter parts without HCV infection. Therefore, screening for and prevention of diabetes in persons with HCV infection could be started earlier than the suggested age of 45 years for the general population, especially for those with higher body mass index levels or with other risk factors for diabetes. In addition, young adults with diabetes in communities with a high prevalence of HCV infection could be tested for an underlying HCV infection. Secondly, the co-morbidity of diabetes and HCV infection at a younger age might exacerbate liver problems because these two conditions augment the progression of hepatic fibrosis and the risk of hepatocellular carcinoma.

Our study also focused on the risk factors responsible for the acquisition of HCV virus by diabetics. In our study, the most frequent risk factor found was history of surgery with 21 (46.7%) followed by history of blood transfusion 13 (28.9%) while history of haemodialysis and tattooing were found to be less common in our study. Transfusion of blood contaminated with HCV was once an important source of transmission. Since 1990, however, the screening of donated blood for HCV antibody has decreased the risk of transfusion-associated HCV infection to less than 1 case in 103,000 transfused units. With the use of more sensitive assays, such as polymerase chain reaction (PCR). The newer assays have decreased the window after infection to 1-2 weeks as reported by Hussain *et al.*, who reported blood transfusion in 13.55% of diabetic patients with HCV positivity[13]. The same study reported that 22.9% of patients who had HCV had a history of any type of surgical procedures which was though less than what was observed in our study but still the top risk factor in their and our study as well.

History of haemodialysis and any type of tattooing are not only rare causes of acquisition of HCV by diabetics in literature but found not too much high in our study too. As reported by Ocak *et al*. History of tattooing was reported in only 10%[14] of patients which was much similar to 8.9% in our study however, they reported history of haemodialysis in 20.8%[5] of patients not much but though a bit higher in what was observed in our study.

CONCLUSION

HCV infection among patients with type 2 diabetes mellitus is still a common problem in our population. We suggest further research work about prevalence and control of other involved risk factors before suggesting guidelines for modifications in the management principles for patients with type 2 diabetes mellitus.

There is a dire need to educate the general population on the dangers and complications of the HCV infection in diabetes. It is also important for all health care providers to come to terms with the early diagnosis and management of this condition in affected patients. However it is highly recommended for more studies to include individuals at greater risk for both HCV infection and type 2 diabetes.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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