ORIGINAL ARTICLE

Frequency of Type 2 Diabetes Mellitus in Patients with Cirrhosis Associated with Chronic Hepatitis C Virus Infection

SOJHLA SALEEM, JAHAN ZAIB, IJAZ HUSSAIN MALIK

ABSTRACT

Objective: To determine the frequency of type 2 diabetes mellitus in patients with cirrhosis associated with chronic HCV infection.
Study design: Descriptive study (case series).
Place and duration of study: Medical unit-I, Nishtar Hospital, Multan from November 1, 2009 to April 30, 2010.
Patients and methods Eighty three (83) patients were included in the study after identification of clinical features of cirrhosis, on detailed history and detailed clinical examination. Relevant investigations, including liver function tests, blood glucose and ultrasonography abdomen was performed.
Results: A total of eighty three (83) cirrhotic patients were included in the study. Thirty patients (30) out of 83 were found to be diabetic i.e., nearly 36% of the patients had developed type 2 diabetes mellitus. Patients in age group of 41 to 60 years had more prevalence of type 2 diabetes mellitus. The duration of cirrhosis was directly proportional to the development of type 2 diabetes mellitus in cirrhotic patients associated with chronic HCV. More precisely, we found that patients having duration of more than 4 years of cirrhosis were prone to become diabetic.
Conclusion: In our group of patients, we determined that there is increased frequency of type 2 diabetes mellitus in patients with cirrhosis associated with chronic HCV infection.
Keywords: Chronic Hepatitis C, Type 2 Diabetes Mellitus, Cirrhosis, Impaired Fasting Glucose,

INTRODUCTION

Hepatitis C is a disease with a significant global impact. According to the World Health Organization there are 170 million people infected with the hepatitis C virus (HCV), corresponding to 3% of the world's total population.**Error! Reference source not found.** There is considerable regional differences. In some countries, e.g., Egypt, the prevalence is as high as 20%[2]. In Pakistan, nearly 10 million people are presumed to be infected with HCV**Error! Reference source not found.**. HCV is a leading cause of cirrhosis in the world[4]. About 30% of patients with cirrhosis have diabetes mellitus (DM)**Error! Reference source not found.**. During the last decade, it has been hypothesized that DM could be one of the extra hepatic conditions attributable to chronic HCV infection. A survey in the United States has shown that patients with age ≥40 years, having chronic HCV infection are more than three times more likely to have type 2 diabetes mellitus than those without HCV infection[6]. Treatment of the diabetes is complex due to liver damage and hepatotoxicity of oral hypoglycemic drugs**Error! Reference source not found.**-**Error! Reference source not found.**-**Error! Reference source not found.**. The patient with cirrhosis and diabetes suffers more frequently from complications of cirrhosis, which can cause death**Error! Reference source not found.**' **Error! Reference source not found.**.

Department of Medicine, Nishtar Medical College/Hospital, Multan
Correspondence to Dr. Sojhla Saleem (Medical Specialist)
Email: dr.aliakbar81@gmail.com

PATIENTS AND METHODS

Patients of any age and gender with chronic HCV infection having cirrhosis were included in the study. Written informed consent was obtained from the patient. All the patients were admitted in the ward through Out-Patient Department (OPD). Investigations such as fasting blood sugar and random blood sugar were carried out at the central laboratory of Nishtar Hospital, Multan.

Data were entered using software SPSS version 11.0. Descriptive statistics were used to calculate mean±standard deviation for age, gender, duration of cirrhosis, fasting blood sugar (FBS) and random blood sugar (RBS). Frequencies were calculated for age, gender and presence of type 2 diabetes mellitus. Stratification was done with regards to age, gender and duration of cirrhosis to see the effect of these on outcomes of the patient. As this was a descriptive study, so test of significance was not used and level of significance (p-value) was not calculated.

RESULTS

A total of eighty three (83) cirrhotic patients were included in the study. The study included 44 (53.01%) male patients, and 39 (46.99%) female patients (Table 3). Mean age was 42.71±14.299 SD, with age range of 16 to 80 years (Table 1). Gender distribution was not significant for development of type 2 diabetes mellitus in cirrhotic patients associated with HCV infection. Mean age for male cirrhotic patients was 42.95±14.24 (SD) years. Moreover, mean age for female cirrhotic patients was 42.44±14.55 (SD) years (Table 4).

Out of these 83 cirrhotic patients, 3 (3.6%) patients were less than 20 years; 35 (42.2%) patients were between 21–40 years; 32 (38.5%) patients were between 41-60 years; 8 (9.6%) patients were between 61 – 70 years; and 5(6%) patients were more than 70 years. The complete age distribution of cirrhotic patients included in this study is shown in (Table 2).

Thirty patients (30) out of 83 were found to be diabetic i.e. nearly 36% of the patients had developed type 2 diabetes mellitus (Table 5). As it can be seen from (Table 6), out of these 30 patients, there were 17 male patients (56.66%) and 13 female patients (43.33%) suffering from type 2 diabetes mellitus in Cirrhosis associated with HCV. Mean age of male diabetic patients in cirrhosis associated with HCV was 48.24±16.20 (SD) years while mean age of female diabetic patients in cirrhosis associated with HCV was 50±17.20 (SD) years. Patients in age group of 41 to 60 years had more prevalence of type 2 diabetes mellitus. In this specific age group, there were 7(23.33%) male patients and 4(13.33%) female patients (Table 6). The complete age distribution of diabetic and non-diabetic patients in cirrhosis associated with chronic HCV according to their gender is shown in Table 6.

Patients having fasting blood sugar (FBS) > 126 mg/dl and random blood sugar (RBS) > 180 mg/dl on two separate occasions were labeled type 2 diabetic (Table 7). According to the above mentioned criteria, out of these 30 type 2 diabetic patients, 2 (6.67%) patients were less than 20 years; 7(23.33%) patients were between 20-40 years; 11(36.67%) patients were between 40-60 years; 6(20%) patients in 61 – 70 years; and 4(13.33%) patients were more than 70 years (Table 7).

Moreover, relationship between developments of type 2 diabetes mellitus in cirrhotic patients associated with HCV and duration of cirrhosis was studied. One (1) patient developed type 2 diabetes mellitus in less than 1 year; four (4) patients developed type 2 diabetes mellitus between 1-2 years; five (5) patients developed type 2 diabetes mellitus between 2-3 years; five patients developed type 2 diabetes mellitus between 3-4 years; seven patients developed type 2 diabetes mellitus between 4-5 years and eight patients developed type 2 diabetes mellitus after 5 years (Fig. 1).

Outcome of the study was that with advancing age and increased duration of cirrhosis, there was increased incidence of type 2 diabetes mellitus in cirrhotic patients associated with chronic HCV. As observed in Table 6 and Figure 1, patients having age between 41 to 60 years and having duration of more than 4 years of cirrhosis, were prone to become diabetic.

Table 1: Age distribution of patients with cirrhosis associated with chronic HCV (n = 83)

N	83
Mean	42.71
Std.Deviation	14.299

Mean age ± SD = 42.71 ± 14.299 years

Table 2 Mean age of cirrhotic patients with chronic hcv included in this study (n=83)

Mean age	**Frequency**	**%age**
<20	3	3.6
25	15	18.1
35	20	24.1
45	22	26.5
55	10	12
65	8	9.6
>70	5	6

In the study, the minimum age was 16 years and maximum was 80 years.

Table 3: Gender distribution of cirrhotic patients with chronic HCV (n=83)

Gender	**n=**	**%age**
Male	44	46.99
Female	39	53.01

Table 4 Gender distribution of cirrhotic patients with chronic HCV according to mean age

Mean Age	**Male**	**%age**	**Female**	**%age**
< 20	1	1.2	2	2.4
25	8	9.6	7	8.4
35	11	13.2	9	10.8
45	12	14.4	10	12.0
55	5	6.0	5	6.0
65	4	4.8	4	4.8
> 70	3	3.6	2	2.4
Total	**44**	**53.01**	**39**	**46.99%**

Mean Age for male patients ± SD =42.95 ± 14.24 years
Mean Age for female patients ± SD = 42.44 ± 14.55 years

Table 5 Distribution of diabetic and non-diabetic cirrhotic patients associated with chronic HCV (n=83)

	Frequency	%age
Non diabetic	53	63.9
Diabetic	30	36.1

Table 6 Gender distribution of diabetic patients in cirrhosis associated with chronic HCV (n=83)

Mean Age	Diabetic	Male	Female
< 20	2	1	1
25	3	2	1
35	4	2	2
45	6	4	2
55	5	3	2
65	6	3	3
> 70	4	2	2

Mean Age of Male Diabetic Patients in Cirrhosis Associated with HCV ± SD = 48.24 ± 16.20 years
Mean Age of Female Diabetic Patients in Cirrhosis Associated with HCV ± SD = 50 ± 17.20 years

Fig.1: Association between Development of Type 2 Diabetes Mellitus in HCV Cirrhotic Patients and Duration of Cirrhosis (n = 30)

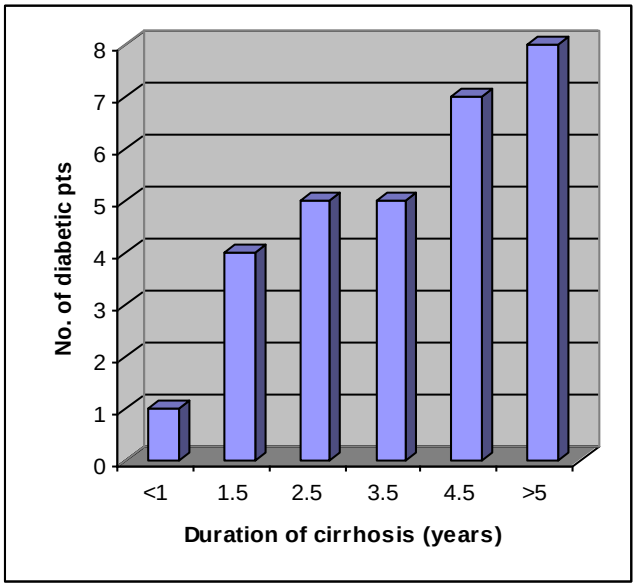

Table 7: Identification of type 2 diabetes mellitus in HCV cirrhotic patients using fasting blood sugar and random blood sugar levels

Mean age of HCV cirrhotic patients	Fasting Blood Sugar (FBS)mg/dl		Random Blood Sugar (RBS)mg/dl	
	100–126	>126	160–180	>180
<20	1	2	1	2
20–40	28	7	28	7
40–60	21	11	21	11
60–70	2	6	2	6
>70	1	4	1	4

DISCUSSION

In our study, thirty (30) out of 83 HCV cirrhotic patients were found to be diabetic i.e. nearly 36% of the patients had developed type 2 diabetes mellitus in cirrhosis associated with chronic HCV infection. In a study conducted by Lecube et al**Error! Reference source not found.**, it was found that when HCV-infected patients with cirrhosis are evaluated, the prevalence of type 2 diabetes is higher than reported in patients with chronic hepatitis, and it ranges from 19.6 to 50%. In another study conducted at USA, the prevalence of type 2 diabetes mellitus associated with HCV infection is 21 to 23%.[11,] **Error! Reference source not found.** In two different studies, one from Korea[12] and other from Egypt**Error! Reference source not found.** found that nearly 25% patients had diabetes mellitus associated with chronic hepatitis C. Another study based in Italy reported 39 % HCV patients had diabetes.**Error! Reference source not found.** In another study conducted on Pakistani population the prevalence of type 2 diabetes mellitus in patients with cirrhosis associated with HCV was 31.25%[13].

In our study, it was observed that patients having age between 41 to 60 years were prone to become diabetic. This result is in accordance with another study conducted in the United States**Error! Reference source not found.** where Mehta et al. have found that patients with age ≥ 40 years, having chronic HCV infection are more than three times more likely to have type 2 diabetes mellitus than those without HCV infection.

In our study, the gender distribution was not significant for development of type 2 diabetes mellitus in cirrhotic patients associated with HCV infection. This is in accordance with Khokhar et al[13] where male and female diabetic cirrhotic patients associated with chronic HCV were equal in number. It is also in accordance with another study which found that gender difference did not explain the increased risk of diabetes in patients with hepatitis C[17].

In our study, we have found that duration of cirrhosis was directly proportional to the development of type 2 diabetes mellitus in cirrhotic patients associated with HCV. More precisely, we found that patients having duration of more than 4 years of cirrhosis were prone to become diabetic. This finding is in concordance with Blanco et al[18] who reported that diabetes manifests clinically as the liver function deteriorates, thus type 2 diabetes mellitus can be considered as an indicator of advanced cirrhosis.

The present study, conducted at Medical Unit I Nishtar Hospital Multan, is unique in its nature as it

reports the prevalence of type 2 diabetes mellitus in patients with cirrhosis associated with chronic HCV infection in Southern Punjab. Although this study is conducted at a regional level, but it can be considered as an indicator of the prevalence of type 2 diabetes mellitus in cirrhotic patients associated with chronic HCV infection in other regions of Pakistan, Moreover, the findings in this study are consistent with the other studies conducted in different developed countries of the world.

CONCLUSION

Many advances have occurred in the clinical care of patients with cirrhosis and the complications of end-stage liver disease. Most of these treatments have focused on the underlying cause of cirrhosis and management of its complications. This study of cirrhotic patients with chronic hepatitis C virus infection has shown increased frequency of type 2 DM in patients with cirrhosis associated with chronic HCV infection. It suggests that persistent and/or active phase of HCV infection play a role in the association with type 2 diabetes mellitus.

REFERENCES

1. Lecube A, Hernandez C, Genesca J, Simo R. Glucose abnormalities in patients with hepatitis C virus infection: epidemiology and pathogenesis. Diabetes Care. 2006;29:1140–9.
2. Anonymous. Hepatitis C: RKI-Ratgeber Infektionskrankheiten. Epidemiologisches Bulletin; 2004.
3. Hamid S, Umar M, Alam A, Siddiqui A, Qureshi H, Butt J. PSG consensus statement on management of hepatitis C virus infection - 2003. J Pak Med Assoc. 2004;54:146–50.
4. Mauss S, Berg T, Rockstroh J, Sarrazin C, Wedemeyer H. Hepatology: a clinical textbook. 2nd ed. Flying Publisher, Germany; 2009: 42. Available from: http://www.hepatologytextbook.com/.
5. Garcia-Compean D, Jaquez-Quintana JO, Gonzalez-Gonzalez JA, Maldonado-Garza H. Liver cirrhosis and diabetes: risk factors, pathophysiology, clinical implications and management. World J Gastroenterol. 2009 Jan;15(3):280–8.
6. Mehta SH, Brancati FL, Sulkowski MS, Strathdee SA, Szklo M, Thomas DL. Prevalence of type 2 diabetes mellitus among persons with hepatitis C virus infection in the United States. Ann Intern Med. 2000;133:592–9.
7. Tolman KG, Fonseca V, Dalpiaz A, Tan MH. Spectrum of liver disease in type 2 diabetes and management of patients with diabetes and liver disease. Diabetes Care. 2007;30:734–43.
8. Holstein A, Hinze S, Thiessen E, Plaschke A, Egberts E. Clinical implications of hepatogenous diabetes in liver cirrhosis. J Gastroenterol Hepatol. 2002;17(6):677–81.
9. Nishida T, Tsuji S, Tsujii M, Arimitsu S, Haruna Y, Imano E, et al. Oral glucose tolerance test predicts prognosis of patients with liver cirrhosis. Am J Gastroenterol. 2006;101:70–5.
10. El-serag HB, Tran T, Everhart JE. Diabetes increases the risk of chronic liver disease and hepatocellular carcinoma. J Gastroenterol. 2004;126:460–8.
11. Mason AL, Lau JYN, Hoang N, Qian K, Alexander GJM, Xu L, et al. Association of diabetes mellitus and chronic hepatitis C virus infection. J Hepatol. 1999;29(2):328–33.
12. Ryu JK, Lee SB, Hong SJ, Lee S. Association of chronic hepatitis C virus infection and diabetes mellitus in Korean patients. Korean J Intern Med. 2001;16:18–23.
13. Khokhar N. Association of chronic hepatitis C virus infection and diabetes mellitus. Pak J Med Res. 2002;41:155–8.
14. Caronia S, Taylor K, Pagliaro L, Carr C, Palazzo U, Petrik J, et al. Further evidence for an association between non-insulin-dependent diabetes mellitus and chronic hepatitis C virus infection. Hepatology. 1999;30:1059–63.
15. El-Zayadi A, Selim O, Hamdy H, Dabbous H, Ahdy A, Moniem S. Association of chronic hepatitis C infection and diabetes mellitus. Trop Gastroenterol. 1998;19:141–4.
16. Macedo G, Ribeiro T. Cirrhosis and diabetes: C the difference. Am J Gastroenterol. 1999;94:3088–9.
17. Zein NN, Abdulkarim AS, Wiesner RH, Egan KS, Persing DH. Prevalence of diabetes mellitus in patients with end-stage liver cirrhosis due to hepatitis C, alcohol, or cholestatic disease. J Hepatol. 2000;32:209–17.
18. Blanco CDV, Gentile S, Marmo R, Carbone L, Coltorti M. Alterations of glucose metabolism in chronic liver disease. Diabetes Res Clin Pract. 1990;8:29–36.