Original Article

Chronic Liver Disease and Its Associations with Hepatitis C Virus in Patients with Type 2 Diabetes Mellitus in Our Setup at DHQTH Bannu

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ABSTRACT

Objective: The objective of this study was to determine chronic liver disease and its association with hepatitis C virus in patients with type 2 diabetes mellitus in our setup at DHQTH Bannu.

Study Design: Descriptive / case series study.

Place and Duration of Study: This study was conducted at the Department of Medicine, DHQ Teaching Hospital (DHDTH) Bannu, Khyber Pakhtunkhwa from Sep 2015 to Sep 2016.

Materials and Methods: Data were collected from 53 patients already diagnosed as Type 2 diabetes mellitus for more than 10 years presented with symptoms and signs of CLD, from Sep 2015 to Sep 2016, through laboratory test, to note their cause of CLD.

Results: Out of 53 T2DM patients, 29 patients were males (54.7%) and 24 (45.3%) were females. All of these were having increase ALT >60 IU/L and increased echogenicity of liver parenchyma. Out of these, 30 patients (56.6%) (19males,11females) were having HCV +ve, 5 patients (9.4%) (3males,2 females) HbsAg +ve, and 3 patients (5.7%) (2males,1female) were B&C -ve. While in the remaining, 3 patients (5.7%) (2males,1female) were having NASH, 2 patients (3.8%)(both females) were AIH(ANA+ve) and 10 patients (18.9%) (3males,7females) were having simple Steotosis (with only increase ALT and increased echogenicity). So overall 30 patients(56.6%) with T2DM with CLD were HCV +ve.

Conclusion: In our set up, the major cause of CLD in T2DM was chronic HCV infection. Most of these patients were cirrhotic, which is an alarming situation and need proper planing by health care providers.

Key Words: T2DM, CLD, Hepatitis C virus (HCV), Cirrhosis , Bannu.

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INTRODUCTION

Type 2 diabetes mellitus is a major Health problem. Rates of diabetes are increasing worldwide. The International Diabetes Federation predicts that the number of people living with diabetes will to rise from 366 million in 2011 to 552 million by 2030.[1]

It is less common in non-Western countries, but as people in these countries adopt Western lifestyles, weight gain, obesity and type 2 diabetes mellitus are becoming epidemic. The top 10 countries in number of people with diabetes are currently India, China, the United States, Indonesia, Japan, Pakistan, Russia, Brazil, Italy, and Bangladesh.[1]

The chronic liver disease is an under diagnosed disease in patients with type 2 diabetes. It ranges from Non Alcoholic Fatty Liver Disease (NAFLD) including Steotosis and Non Alcoholic Steoto Hepatitis (NASH), then infective hepatitis caused by HCV or HBV, and sometimes other causes including autoimmune hepatitis. Out of these, the infective causes both HCV and HBV are more important, because that can be screened and treated.

Hepatitis C and B are major world health problem. Worldwide, more than 170 million persons have hepatitis C virus (HCV) infection,[2] of whom 71 million have chronic infection.[3] In Pakistan, its prevalence is 4.8%[4]. In Khyber Pakhtunkhwa (KPK) and FATA areas which are drained to our set up, it is reported even high (up to 6.93%)[5,6].HBV is also endemic here. In Pakistan its prevalence is 2.4%[7], while in KPK and FATA, it is up to 4.49%[5].

There is a two way association between T2DM and

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HCV. Both are prevalent diseases worldwide[1,2,3] and are associated with increased morbidity and mortality.

On one hand, there is increased risk for T2D in patients with chronic HCV infection [8] esp when there is liver dysfunction [9].While insulin resistance (IR) and T2DM are more frequently reported as complications of HCV infection, HCV is also known to be associated with several autoimmune manifestations, including type 1 diabetes mellitus (T1DM)[10,11]. Therapy for chronic HCV infection, in particular interferon alpha (IFNα) can also trigger diabetes, as IFNα can induce or exacerbate autoimmune diseases such as T1DM[12]. Cirrhosis itself is "diabetogenic" with various studies describing the majority of cirrhotics as having impaired glucose tolerance[13,14,15]. T2DM was significantly higher among patients with HCV cirrhosis than in patients with cirrhosis due to other etiologies[14]. HCV infection precedes the diagnosis of T2DM in as many as 73% of cases, further suggesting HCV's pathogenic role in the development of T2DM[16,17,18]. It is estimated that up to 33% of chronic hepatitis C patients have T2DM[19]. There is significantly higher risk for T2DM in HCV patients are compared to hepatitis B virus (HBV)[8] and 2- to 10-fold increase of T2DM in chronic HCV infection compared to other liver diseases[19,20,21,22,]. It is also estimated that 20% of chronic HCV patients will develop cirrhosis and as many as ~50% of these patients will have T2DM[14,23].

On the other hand,T2DM is a predisposing factor for HCV infection[24,25,26]. Also Insulin Resistance (IR) and T2DM have a negative impact on clinical outcomes for patients with chronic HCV infection, including reduced rate of sustained virological response (SVR), progression to fibrosis and cirrhosis, and higher risk for development of hepatocellular carcinoma (HCC).

Unfortunately, no local data is available regarding chronic liver disease in T2DM patients and its association with HCV, in out set up. This is a randomized study at smaller scale which can later be applied at larger scale. Also due to many reasons such as lack of awareness, limited resources, and no cost-free screening campaign for adults, the early diagnosis and prompt treatment of viral hepatitis in not satisfactory in Khyber Pakhtunkhwa, even in high risk people, to prevent chronic liver disease and cirrhosis. HCV is a treatable disease. With the standard therapy having combination, 50–80% of people treated are cured[4]. Genotype 2&3 are common in Pakistan who show sustained response to treatment in 70-80%[27].

Keeping this in mind the following study was designed to see CLD in T2DM and its association with HCV in our community.

MATERIALS AND METHODS

This descriptive, case series study was carried out at Department of Medicine, DHQ Teaching Hospital Bannu KPK, **12** months from Sep 2015 to Sep 2016.

Sample Size: 53 patients already diagnosed as T2DM for more than 10 years, now having CLD, were analyzed for causes of CLD.

Sampling Technique: Consecutive, Non-probability Sampling.

Inclusion Criteria: All "T2DM" patients diagnosed for more than 10 years (noted from clinical record/History), of Either gender, aged above 40 and under 65 years, having CLD (increase ALT >60 IU/L plus increase echogenicity of liver parenchyma on ultrasound abdomen, present for >6months).

Exclusion Criteria: Those patients who were not filling the inclusion criteria, with a history of previous Hepatitis C infection/treatment, patients with End-stage liver disease, patients terminally ill, patients who were not willing to be included in study, and patients with dementia/mentally retarded were not included because, as they were either already infected and treated, would not benefit from future planned screening/treatment or would give recall bias. If included in the study, these would act as confounders to introduce bias in the study results.

Data Collecting Procedure: The study was conducted after approval from hospitals ethical and research committee/ board. All the patients who were T2DM and meeting the inclusion criteria, as per operational definitions, presented to the Department of Medicine, DHQ Teaching Hospital Bannu, through emergency or OPD, were included in the study. All patients were first counseled for interview. The purpose and benefits of the study were explained to all patients, and a written informed consent was obtained from all who agreed to participate in the study. A detailed medical history was taken from all the patients, regarding duration of T2DM and previous HCV infection for cause of high ALT and increase echogenicity of liver parenchyma. Then these patients (study population) were screened for HCV by ELISA (used as a diagnostic tool) and their status noted on flow sheet as data collection tool having all variables of interest.

All the patients were categorized as having Simple Fatty Liver/Steotosis, NASH, HCV related CLD, HBV related CLD, B/C negative CLD and Auto-immume Hepatitis if ANA+ve. All the information including name, age, gender, address, disease status were recorded in that pre-designed Proforma. Only a complete Proforma was subjected to analysis. Strict exclusion criteria was applied to control confounders and bias in the study results.

Statistical Analysis: Data obtained was entered into SPSS version 23 and analyzed in descriptive statistics. Mean $\pm$ SD were calculated for numerical/ quantitative variables like age. Frequencies and percentages (%) were calculated for categorical/ qualitative variables such as gender, disease status. Disease status were stratified among age and gender to see the effect modifiers. All results were presented in the form of tables, charts.

RESULTS

A total of 53 patients with T2DM were included in the study. Out of 53 T2DM patients, 29 patients were males (54.7%) and 24 (45.3%) were females, with male to female ratio of 1.21:1.0. Their age ranged between 45 and 64 years, and the mean age was 54.19±5.027 years. All of these were having increase ALT >60mg and increased echogenicity of liver parenchyma. Out of these, 30 patients (56.6%) (19 males, 11 females) were having HCV +ve, 5 patients (9.4%) (3males,2females) HbsAg +ve, and 3 patients (5.7%) (2males,1female) were B&C -ve. While in the remaining, 3 patients (5.7%) (2males,1female) were having NASH, 2 patients (3.8%)(both females) were AIH(ANA+ve) and 10 patients (18.9%) (3males, 7females) were having simple Steotosis (with only increase ALT and increased echogenicity).

So overall 30 patients(56.6%) with T2DM with CLD were HCV +ve.

Summarized Descriptive statistics of the study population are shown in tables and charts.

Table No.1:Age Distribution of Study Population (N=53):

Age group	Frequency	Percent
41-50Years	15	28.3
51-60Years	32	60.4
>60 Years	6	11.3
Total	53	100.0

Parameters	Total No of patients	Minimum (years)	Maximum (years)	Mean	Std. Deviation
Age in years	53	45.00	64.00	54.19	5.027

Table No.2: Gender distribution of study population (N=53)

Gender	Frequency	Percent	Valid Percent	Cumulative Percent	"p" value
Male	29	54.7	54.7	54.7	0.05
Female	24	45.3	45.3	100.0	
Total	53	100.0	100.0		

Table No.3; Frequency of diseases of patients (N=53)

Diseases	Frequency	Percent	Valid Percent	Cumulative Percent
Steotosis	10	18.9	18.9	18.9
NASH	3	5.7	5.7	24.5
HCV+	30	56.6	56.6	81.1
HBS+	5	9.4	9.4	90.6
B&C -ve	3	5.7	5.7	96.2
AIH (ANA+)	2	3.8	3.8	100.0
Total	53	100.0	100.0	

Table No.4: Gender wise distribution of diseases in patients (N=53) :

Gender	Disease						Total
	Steotosis	**NASH**	**HCV+**	**HBS+**	**B & C -ve**	**AIH (ANA+)**	
Male	3	2	19	3	2	0	29
Female	7	1	11	2	1	2	24
Total	**10**	**3**	**30**	**5**	**3**	**2**	**53**

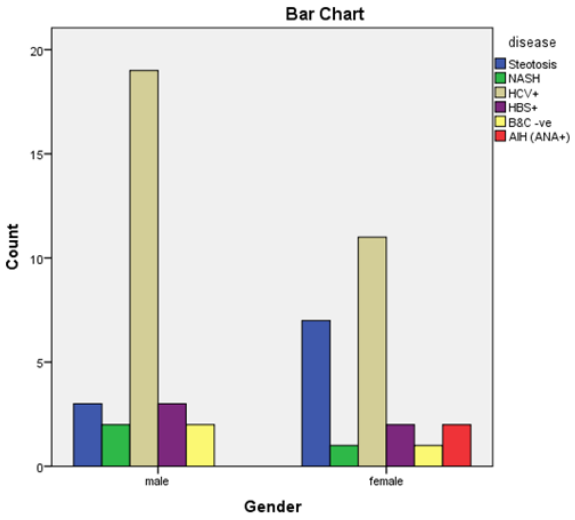

Figure No.1: Gender wise distribution of diseases in patients (N=53):

DISCUSSION

A total of 53 patients with T2DM were included in this study. Out of 53 T2DM patients, 29 patients were males (54.7%) and 24 (45.3%) were females. All of them were having increase ALT >60 IU/L and increased echogenicity of liver parenchyma on Ultasound Abdomen. When screened for viral hepatitis by Elisa, 30 patients (56.6%) (19 males,11 females) came out to be HCV +ve (also confirmed later by PCR) , and 5 patients (9.4%) (3 males,2 females) were HbsAg +ve, while the remaining only 18 patients were negative for viral hepatitis. It showed that viral hepatitis is more common here, and it is the common cause of CLD in T2DM patients having diabetes for more than 10 years, where it contributed to 66% collectively. In these patients those having HCV, majority were early cirrhosis on ultrasound abdomen, they were male, and their glycaemic control was not good. It means that diabetes with poor control has added to early and accelerated fibrosis and cirrhosis. One reason of this high prevalence of viral hepatitis in our setup is that patients are also drained from adjacent FATA area, where hepatitis B is more commonly noted.

The remaining 18 patients negative by Elisa for HBV and HCV, were further assessed for cause of increase ALT >60 IU/ml and increased echogenicity of liver

parenchyma on Ultasound Abdomen, including HBc (core) antibodies (for occult HBV), AST level and ANA , and then labeled B&C -ve, AIH, NASH or simple Fatty liver (steotosis). NASH was simply labeled on basis of increase ALT and AST levels with ALT/AST ratio <1, with no history of alcohol with no other obvious cause for increase liver enzymes, but without liver biopsy (being invasive and not available here in our setup).

This study was a preliminary randomized study in this area and on small scale which can later be applied at larger scale. It presents 53 T2DM patients who were diabetic for >10years,presented with CLD, both out patients and in-door patients, who were aged 45 and 64 years, and the mean age was 54.19±5.027 years 1-60 years. Out of these, a large portion of 35 patients(66%) were having viral hepatitis, and 30 patients HCV (56.6%), most of them were male and having early cirrhosis, though HCV can be prevented by adopting preventive measures, easily early diagnosed and promptly treated to prevent cirrhosis. This was partially because of lack of awareness/ education on part of the patients, lack of proper counseling/educating session on part of health care providers, and lack of support services and cost free screening programs for diabetic population on part of the government.

CONCLUSION

This study has demonstrated that CLD in T2DM patients was mainly because of viral hepatitis in our set up, where both the viruses have high prevalence, mainly because of HCV and they were male predominate and having early cirrhosis at presentation, all these were having poor glycaemic control.

Therefore, all those managing T2DM patients should also counsel and educate the patients, regarding preventive measures against both HCV & HBV infections, screen these patients for viral hepatitis, and if infected with HCV, then promptly treat them with standard Treatment including recent antivirals for HCV, to prevent CLD and cirrhosis. It is essential for physicians caring for HCV patients to be aware of the high risk for T2DM (and T1DM) and that they screen HCV patients for diabetes. In addition, the presence of diabetes in an HCV patient alert the clinician for the possibility of worse outcomes of HCV infection.

Recommendations: All the T2DM patients should be screened for viral hepatitis especially HCV to start prompt treatment to prevent CLD and cirrhosis, meanwhile also have a good glycaemic control to improve the treatment outcomes including End of Treatment response. Moreover all the HCV free-treatment programs, which have already been started, should incorporate free screening program.

Author's Contribution:

Concept & Design of Study:	Raza Muhammad Khan
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Revisiting Critically:	Raza Muhammad Khan
Final Approval of version:	Raza Muhammad Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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