

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

Muhammad Sohrab Khan¹, Gohar Ali Khan^{1✉}, Umair Amir Khan², Saba Shams²

1. Department of Medicine, Bannu Medical College, Bannu, Khyber Pakhtunkhwa, Pakistan.

2. Department of Medicine, Bacha Khan Medical College, Mardan, Khyber Pakhtunkhwa, Pakistan.

ABSTRACT

The objective of this study was to determine the frequency of Type 2 Diabetes Mellitus (DM) in patients with Hepatitis C Virus (HCV) infection. This cross-sectional study was conducted at the Bacha Khan Medical College, Mardan, over a period of 6 months. A total of 300 patients with HCV PCR positive were selected via a non-probability convenient sampling technique. Patients were evaluated for type 2 DM using fasting blood sugar and HbA1c test. The patient's age ranged from 30 to 75 years of age. SPSS-20 was used for statistical analysis. We found a 28% prevalence of type 2 DM in HCV patients. The mean age of the patients was 44.78 ± 10.7 . Among the total number of patients, 37.7% were females and 62.7% were males. Patients were divided into two age groups: (1) 30 to 40 and (2) patients greater than 40 years of age. We found a higher number of HCV patients in age group 2, which was 178 (59.3%). There was no statistical significance of Type 2 DM with gender, while age was found to be significant. We concluded that HCV patients are at a higher risk of having Type 2 DM, and increasing age is a major contributor to Type 2 DM in HCV patients.

KEY WORDS: Type 2 Diabetes Mellitus, Hepatitis C Virus, Patients, Seropositive

INTRODUCTION

Hepatitis C (HCV) is known as a liver disease caused by a virus and can lead to acute, chronic, or severe hepatitis. Depending on the severity, it can be categorized as a mild (can last for a few weeks) or severe (long-lasting) disease. No vaccine is available for HCV. Chronic HCV could result in deadly liver cancer. The prevalence of HCV patients leading to chronic infections is 85%¹. HCV usually spreads through blood transfusion, most probably with the use of unsafe injections, unsafe sex, and untested blood transfusion. The HCV infection is spreading rapidly, and it has affected more than 177.5 million patients around the world². A huge number of people who develop chronic HCV will advance towards liver cancer (cirrhosis) and hepatocellular carcinoma.

Factors like sex, obesity, age, alcohol consumption, and co-infections contribute to the development of the cirrhotic stage³⁻⁴. Diabetes Mellitus (DM), also known as blood sugar, is a condition when the body fails to utilize glucose; as a result, the glucose level starts rising. A hormone known as insulin is responsible for controlling the glucose level in the blood, which is created by the pancreas. An increase in glucose levels in the blood may trigger symptoms like excessive urination, gradual weight loss, and thirst. DM is one of the deadliest factors contributing to the death toll worldwide, resulting in mortality > 8% globally⁵. If DM is left unchecked, various life-threatening problems might arise, i.e., nerve damage (associated with patients having a history of diabetes affected by peripheral neuropathy leading to hand or leg amputation), cardiac diseases, retinopathy, weakened immunity, etc⁶. DM is considered to be a serious disease and can take a life if not properly addressed during pregnancy⁷. Studies say that Pakistan will achieve the top most position in the worldwide categorization of patients affected by diabetes in the year 2030 for the age group of 20–79, with more than 13 million diabetic patients⁸. In DM patients, there are two possibilities: the body stops producing insulin (T1DM) or the body's response to insulin is improper (T2DM). Patients with T2DM can create insulin, but the body fails to respond properly, so glucose is less able to enter the cells, and the problem arises known as Insulin Resistance (IR). Pancreases work extremely hard to create more insulin to control glucose levels but fail due to the presence of a high amount of sugar in the blood⁹. Several studies reported that HCV infection may also contribute to the development of diabetes,

and a higher prevalence of type 2 diabetes mellitus has been observed in the developed world (2% to 9.4%) in patients with HCV infection than in those with other forms of chronic hepatitis¹⁰. This association between HCV infection and diabetes was made for the first time by Sasso et al. in 2021¹¹. Since then, a number of observational studies have been published. There are several organized factors that influence the development of diabetes among HCV-infected patients, like age, sex, family history of diabetes, African-American race, and HIV coinfection. Insulin resistance (IR) and diabetes can develop at any stage of HCV infection. Multiple mechanisms have been accounted for insulin resistance and the development of diabetes in patients with chronic hepatitis C. It promotes IR mainly through interfering with the insulin signaling pathway in hepatocytes, increasing the inflammatory response with the production of cytokines such as TNF-alpha and IL-6, and increasing oxidative stress¹⁰. There have been many studies in the past on the frequency of diabetes in HCV infections. Italy showed a prevalence of 7.6% in T2D patients with HCV¹². A Pakistani study presented the same trend, with a prevalence of slightly more than 3% in type 2 DM patients infected by HCV¹³. Chronic infection with HCV alone hit the vast population of Pakistan, with a prevalence of 10%¹⁴. Another study showed the frequency of HCV infection in China was 3.2% and in Egypt was 22%¹⁵. HCV infection and type 2 diabetes mellitus are two chronic conditions that contribute to significant morbidity and mortality. The rationale behind this study is to find out the maximum number of cases of type 2 diabetes in those patients who are infected with the hepatitis C virus. The objective of this study was to determine the frequency of Type 2 Diabetes Mellitus (DM) in patients with Hepatitis C Virus (HCV) infection. In this way, we will establish a valid association between type 2 diabetes and the HCV seropositive population.

MATERIAL AND METHODOLOGY

This cross-sectional study was conducted at the Bacha Khan Medical Complex in Swabi after getting permission from the hospital's ethical committee. A total of 300 patients were selected using the Openepi sample calculator. A non-probability convenient sampling technique was used. The duration of the study was 6 months. Patients aged 30 to 75 with HCV PCR positives were included in the study. Patients were divided

included in the study. Patients were divided into two age groups: (1) 30 to 40 and (2) patients greater than 40 years of age. Patients with a random blood glucose level > 140 mg/dl were confirmed to be type 2 diabetic. Patients with diabetes who were less than 30 years old and patients with hepatitis C and B simultaneously were excluded. SPSS-20 was used for statistical analysis. A chi-square test was utilized to determine the association of categorical variables like age and gender with type 2 DM in HCV-positive patients. A P-value of 0.05 in the Chi-Square test was considered to be statistically significant.

RESULTS

Among total number of patients, mean age of the patients was 44.78 ± 10.7 . The age ranged from 30 to 75 years (Table 1).

TABLE 1: THIS TABLE INDICATES RANGE AND MEAN AGE OF PATIENTS

	N	Minimum	Maximum	Mean	Std. Deviation
Age	18	75	46.43	16.133	10.667

There were 37.3% females and 62.7% males (Table 2). We found a prevalence of 28% of Type 2 diabetes in patients with HCV (Table 3).

TABLE 2: THIS TABLE INDICATES FREQUENCY AND PERCENT OF GENDER

Gender	Frequency	Percent
Female	112	37.3
Male	188	62.7
Total	300	100.0

TABLE 3: THIS TABLE INDICATES PREVALENCE OF TYPE 2 DM

Result	Frequency	Percent
Non Diabetic	216	72.0
Type 2 Dm	84	28.0
Total	300	100.0

Patients were divided in two age groups, one having age groups from 30 to 40 and other greater than 40 years of age. We found higher number of HCV patients in the age group greater than 40 years of age which were 178 (59.3%) (Table 4).

TABLE 4: THIS TABLE INDICATES PREVALENCE OF HCV PATIENTS BETWEEN TWO AGE GROUPS

Age Groups	Frequency	Percent
>40	178	59.3
30 to 40	122	40.7
total	300	100.0

The results of chi-square to find the association between age and type 2 DM indicates the significant relation between them i.e. p-value 0.001 as indicate in Table 5.

TABLE 5: THIS TABLE INDICATES THE ASSOCIATION BETWEEN AGE AND TYPE 2 DM THROUGH CHI-SQUARE.

Age Groups	Result		Total
	Non Diabetic	T2DM	
>40	105	73	P= 0.001
	59.0%	41.0%	
30 to 40	111	11	
	91.0%	9.0%	
	216	84	
total	72.0%	28.0%	

We found no association between gender and Type 2 Diabetes in patients with HCV, upon applying chi-square test. The P-value was greater than 0.05 which depicts no statistical significance (Table 6).

TABLE 6: CHI-SQUARE TEST SHOWING NO SIGNIFICANCE BETWEEN GENDERS AND TYPE 2 DM

Gender	Result		Total
	Non Diabetic	T2DM	
Female	73	39	P= .042
	65.2%	34.8%	
Male	143	45	
	76.1%	23.9%	
	216	84	
Total	72.0%	28.0%	

DISCUSSION

Our study showed a prevalence of 28% of DM Type 2 in HCV patients. Similar prevalence has been shown in other studies conducted in Pakistan^{16,17}. In studies conducted in North America, the Middle East, Asia, and Europe, the prevalence was found to be between 13% to 33%¹⁸. In this way, 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 DM 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 in either a direct or indirect way. Secondly, a major contribution of already present risk factors for diabetes, such as positive family history and advancing age, also plays an important role among HCV-infected persons¹⁰. In our study, we observed that age is an important factor for type 2 DM in HCV patients. As age increases, the risk of type 2 DM also increases in HCV patients. We have found that 41% of HCV patients with Type 2 DM were in the age group greater than 40 years of age. Similar findings have also been observed in various studies^{19,20}. In our study, the association between age and Type 2 DM in HCV patients was statistically significant ($p = 0.001$), which is in accordance with another study. We did not find any association between gender and type 2 DM in patients with HCV ($p = 0.042$). Similar findings were also observed in other studies¹⁰. There are certain limitations to this study. The most important limitations of this study are the small sample size, single-centered, hospital-based study, and only including HCV seropositives, which may not reflect the actual incidence of type 2 diabetes in HCV seropositives.

CONCLUSION

This study concludes that there is a strong association of type 2 DM with HCV infection. Odds of development of type 2 diabetes increases by two folds if an HCV patient has cirrhosis. Patients having HCV are at greater risk of having insulin deficiency at later age. Age was found significant while gender had no relation with type 2 in HCV patients. Type 2 diabetes can negatively affect the outcome of HCV which can lead to liver cirrhosis and eventually cancer.

Physicians involved in the treatment of HCV patients need to be aware of the risk of type 2 diabetes in their patients. It is necessary to screen and control earlier for the presence of type 2 DM and also rule out HCV infection among diabetic populations which is rarely done on population-based studies.

REFERENCES

- de Mattos ÂZ, Debes JD, Boonstra A, Yang JD, Balderramo DC, Sartori GD, de Mattos AA. Current impact of viral hepatitis on liver cancer development: The challenge remains. *World journal of gastroenterology*. 2021 Jun 28;27(24):3556.
- Tariq M, Shoukat AB, Akbar S, Hameed S, Naqvi MZ, Azher A, Saad M, Rizwan M, Nadeem M, Javed A, Ali A. Epidemiology, risk factors, and pathogenesis associated with a superbug: A comprehensive literature review on hepatitis C virus infection. *SAGE Open Medicine*. 2022 Jun;10:20503121221105957.
- Lampimukhi M, Qassim T, Venu R, Pakhala N, Mylavarapu S, Perera T, Sathar BS, Nair A, Lampimukhi Jr M, Pakhala Jr N. A review of incidence and related risk factors in the development of hepatocellular carcinoma. *Cureus*. 2023 Nov 26;15(11).
- Garrido-Esteva M, Herruzo R, Flores-Herrera J. Co-infections, comorbidities, and alcohol or other substances abuses in chronic hepatitis C-related hospitalisations in Spain. *Gastroenterología y Hepatología*. 2022 Nov 1;45(9):677-89.
- World Health Organization. Global report on diabetes. Geneva: World Health Organization; 2016.
- Papatheodorou K, Papanas N, Banach M, Papazoglou D, Edmonds M. Complications of diabetes 2016. *J Diabetes Res*. 2016; 2016: 6989453.
- Buchanan TA, Xiang AH, Page KA. Gestational diabetes mellitus: risks and management during and after pregnancy. *Nat Rev Endocrinol*. 2012 Nov;8(11):639–49.
- The International Diabetes Federation, Atlas of Diabetes Sixth Edition. Retrieved from URL http://www.idf.org/sites/default/files/Atlas-poster-2014_EN.PDF. Accessed on 28th December 2014.
- Wang CS, Wang ST, Yao WJ, Chang TT, Chou P. Community-based study of hepatitis C virus infection and type 2 diabetes: an association affected by age and hepatitis severity status. *Am J Epidemiol*. 2003;158:1154-60.
- Memon MS, Arain ZI, Naz F, Zaki M, Kumar S and Burney AA. Prevalence of Type 2 Diabetes Mellitus in Hepatitis C Virus Infected Population: A Southeast Asian Study. *Journal of Diabetes Research* 2013(4):539361.
- Sasso FC, Pafundi PC, Caturano A, Galiero R, Vetrano E, Nevola R, Petta S, Fracanzani AL, Coppola C, Di Marco V, Solano A. Impact of direct acting antivirals (DAAs) on cardiovascular events in HCV cohort with pre-diabetes. *Nutrition, Metabolism and Cardiovascular Diseases*. 2021 Jul 22;31(8):2345-53..
- Jadoon NA, Shahzad MA, Yaqoob R, Hussain M, Ali N. Seroprevalence of hepatitis C in type 2 diabetes: evidence for a positive association. *Virology* (2010) 7:304.
- Idrees M, Riazuddin S. A study of best positive predictors for sustained virologic response to interferon alpha plus ribavirin therapy in naive chronic hepatitis C patients. *BMC Gastroenterol*. 2009;9:5-13.
- Ayoub H, Al Kanaani Z, Abu-Raddad LJ. 2018 Characterizing the temporal evolution of the hepatitis C virus epidemic in Pakistan. *J. Viral Hepat*. Epub ahead of print.
- World Health Organization. Global burden of disease (GBD) for hepatitis C. *J Clin Pharmacol* 2004; 44:20–9.
- Rafique B, Amir M, Khaskheli AJ, Arshad AR, Aslam A, Irfan M. Association of Type 2 Diabetes Mellitus with Chronic Hepatitis C Virus Infection. *Pakistan Armed Forces Medical Journal*. 2022 Feb 28;72(1).
- Ahmad HA, Saleem T, Saim M, Farzand A, Ahmad I. A review on the prevalence of Hepatitis C virus in diabetic patients in different regions of Pakistan. *Ann. For. Res*. 2022;65(1):10198-218.
- Hammerstad SS, Grock SF, Lee HJ, Hasham A, Sundaram N, Tomer Y. Diabetes and hepatitis C: a two-way association. *Frontiers in endocrinology*. 2015 Sep 14;6:134.
- Angel M, Petrosyan Y, Doyle MA, Cooper C. HCV infection characteristics, treatment uptake and outcomes in patient with diabetes mellitus. *BMC Endocrine Disorders*. 2022 Nov 12;22(1):277.
- Cacciola I, Russo G, Filomia R, Pitrone C, Caccamo G, Giandalia A, Alibrandi A, Stella Franzè M, Porcari S, Maimone S, Saïta C. Over time evaluation of glycaemic control in direct-acting antiviral-treated hepatitis C virus/diabetic individuals with chronic hepatitis or with cirrhosis. *Liver International*. 2021 Sep;41(9):2059-67.

Address for Correspondence:

✉ Assistant Professor Department of Medicine, Bannu Medical College, Bannu, Khyber Pakhtunkhwa, Pakistan.
 @ alidurrani.dr2003@gmail.com
 ☎ 0317-9553864

Received: March 17, 2024 , Revised: Aug 19, 2024, Accepted: Oct 22, 2024

Contribution of Authors:	
CONTRIBUTION	AUTHOR ABBREVIATION
Conception & Planning of the Research	MSK, GAK, UAK
Active Participation in Methodology	MSK, UAK, SS
Interpretation Analysis & Discussion	MSK, GAK

CONFLICT OF INTEREST

None Declared

GRANT SUPPORT AND FINANCIAL DISCLOSURE

NIL

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.