

# Frequency Of Hepatitis C Infection in Diabetes Mellitus

M A QAZI M FAYYAZ G M U D CHAUDHARY A JAMIL A H MALIK A I GARDEZI M H BUKHARI

Department of Medicine, Quaid-e-Azam Medical College, Bahawalpur.

Correspondence to Dr Masroor Ali Qazi Associate Professor of Medicine

**Place and duration of study:** The study was conducted at diabetic clinic B.V. Hospital/Q.A.M.C Bahawalpur from December 1<sup>st</sup>, 2004 to March 15<sup>th</sup>, 2005. **Background:** Diabetes mellitus and hepatitis C infections are common and emerging problems of the society. Either diabetes mellitus is common in chronic hepatitis C patients as reported initially by Ellison and co-workers or hepatitis C infection is more frequent in diabetes mellitus. We want to study the frequency of hepatitis c infection in diabetes mellitus. **Objectives:** To study the frequency of hepatitis C infection in diabetic patients and to note any risk factors of diabetic patients predisposing to hepatitis C infection. **Designs:** A cross-sectional-Observational-descriptive analytic study. **Subjects and Methods:** A total of 250 consecutive diabetic patients of either sex were compared with 6574 blood donors for hepatitis c infection. They were evaluated for hepatitis C infection by using Enzyme Linked Immunosorbant Assay (ELISA-3) which is an anti-HCV antibody test. On basis of this test, the patients were divided into two groups, anti-HCV +ve and anti-HCV -ve. Different variables of these patients were studied and compared in these two groups. Variables studied were as follows:- Age, Sex, BMI, Mode of therapy area of their residence(rural or urban) Duration of diabetes mellitus, Blood pressure, Nephropathy and Control of diabetes mellitus. **Results:** Among a total of 250 patients, 120 (48%) were male and 130 (52%) were female. Two hundred and forty-four (97.6%) patients were of type-II DM and 06 (2.4%) patients were of type-I DM. 22 (8.8%) patients were on insulin therapy while 228 (91.2%) were on oral hypoglycemic agents. Anti-HCV test was positive in 69 (27.6%) diabetic patients as compared to blood donors 41(0.62%). In anti-HCV positive group, longer duration of diabetic mellitus (<one yr 20.28%, 1-15 yrs 63.76%, >15yrs 15.94%), poor control of diabetic mellitus(87%), insulin therapy(17.39%) hypertension(91.3%) and nephropathy(94.2%) were the significant variables while BMI, age, sex and whether they were belonging to either rural or urban area were not significant in both the groups. **Conclusion:** Hepatitis C infection is common in diabetic patients as compared to control group (27.6% vs 0.62%). Out of diabetic patients HCV infection is more common with longer duration of diabetic mellitus, poor control of diabetic mellitus, hypertension, nephropathy and insulin therapy.

**Key Words:** Anti-HCV. Diabetes Mellitus. Hepatitis C Infection. Nephropathy.

Hepatitis C infection has been recognized a major public health problem all over the world<sup>(1)</sup>. Worldwide prevalence is 3%, while the prevalence in Pakistan is 4-7%<sup>2</sup>. Hepatitis C infection is asymptomatic not only in chronic but also in acute stage<sup>3</sup>. It leads to chronic liver disease in 60% and leading to liver cirrhosis in 10-20 years<sup>4</sup> And hepatocellular carcinoma is an important complication of liver cirrhosis developing at the rate of 1-4% per year<sup>5,6</sup>. On the other hand, diabetes mellitus is also a major public health problem. Worldwide prevalence of diabetes is 4%, while in Pakistan prevalence of diabetes is 4.5-11% making Pakistan 6<sup>th</sup> in world ranking of diabetes mellitus prevalence<sup>7,8</sup>. The spectrum of liver disease in type-II diabetes ranges from nonalcoholic fatty liver disease to cirrhosis and hepatocellular carcinoma and liver disease is one of the leading causes of death in persons with type-II diabetes<sup>9</sup>. Nonalcoholic fatty liver disease is now considered part of the metabolic syndrome, and, with alcohol and hepatitis C, is the most common cause of chronic liver disease in the United States<sup>9,10,11,12</sup>. When two diseases are common in the community then chances of association are very high, many studies are in favour of association between diabetes mellitus and hepatitis C infection<sup>13,14</sup>. Either diabetes mellitus is common in chronic hepatitis C patients or hepatitis C infection is more frequent in diabetes mellitus this controversy is still going on<sup>15,16</sup>. We have conducted a study to see frequency of

hepatitis C infection in diabetes mellitus and to note any risk factor of diabetic patients predisposing to hepatitis C infection

## Place and duration of study:

The study was conducted at diabetic clinic B.V. Hospital/Q.A.M.C Bahawalpur from December 1<sup>st</sup>, 2004 to March 15<sup>th</sup>, 2005.

## Objectives:

To study the frequency of hepatitis C infection in diabetic patients and to note any risk factors of diabetic patients predisposing to hepatitis C infection.

## Designs:

A cross-sectional-Observational descriptive study.

## Subjects and Methods:

Two hundred and fifty known diabetic patients of either sex were evaluated for hepatitis C infection by hepatitis C Virus One Step Test Device This screening test was chromatographic immunoassay for the qualitative detection anti-HCV antibody in serum or plasma (relative sensitivity:96.8%, relative specificity: 99%, Accuracy:98.9%) Anti-HCV positive patients by this screening test were subjected to enzyme linked immunosorbant assay (ELISA-3) for confirmation, This test (ELISA-3) was performed with AXSYM HCV version 3.0 which was based on Microparticle Enzyme Immunoassay (MEIA) technology (relative sensitivity:

100%, relative specificity:99.8%). On basis of this test, the patients were divided into two groups, anti-HCV positive and anti-HCV negative. Different variables of these patients were studied and these two groups were compared for statistical significance. Chi-Square was applied to the asses the statistical significance and P value > 0.05 was considered as significant. Variables studied were as follows:- Age, Sex, BMI (normal < 25, overweight > 25), Rural / urban residents, Mode of therapy ( oral therapy or insulin injection),duration of diabetes mellitus, Blood pressure ( normotensive < 140 / 80 mmHg, hypertensive > 140/80 mmHg), Nephropathy (micro-albuminuria / macroalbuminuria), Control of diabetes mellitus( FBS < 7.8 mmol/l –optimal control, & FBS >7.8 mmol/l – poor control).

### Results:

Among a total of 250 patients, 120 (48%) were male and 130 (52%) were female. Two hundred and forty-four (97.6%) patients were of type-II DM and 06 (2.4%) patients were of type-I DM table no.1. Twenty-two (8.8%) patients were on insulin therapy while 228 (91.2%) were on oral hypoglycemic agents.

Anti-HCV test is positive in 69 (27.6%) patients. The age distribution is from 22 to 100 years. The most of the patients are in age group > 50 years as shown in table no.2. There are 39 (56.5%) male and 30 (43.5%) female, thirty seven patients (53.62%) were either overweight, and majority of the patients are belonging to urban area. Duration of diabetes mellitus was < 1 year in 14 (20.28%) patients, 1-15 years in 44 (63.76%) patients and > 15 years in 11 (15.94%) patients, uncontrolled DM in 60 (87%) patients, nephropathy in 65 (94.20%), systemic hypertension in 63 (91.30%) patients and 12 (17.39%) patients were on insulin therapy.,

Comparison of patients with anti-HCV +ve and anti-HCV –ve group revealed that maximum no of patients in each group is in > 50 years as shown in table no.1, statistically insignificant difference are noted in each group. Male are comparatively more in anti-HCV +ve group but insignificant statistically. Similarly overweight patients are more common in anti-HCV +ve but again it is statistically insignificant. Similarity rural / urban background is also insignificant. Frequency of anti-HCV +ve patients is more with longer duration of diabetes mellitus which is statistically significant (P < 0.5). Control of diabetes mellitus is an important factor as Anti-HCV +ve patients are with poor control (p < .001). Insulin therapy is also significant statistically in anti-HCV +ve group (P < .005). Nephropathy and hypertension are also more common in anti-HCV +ve group (P < .01 in both).

### Discussion:

In our study frequency of hepatitis C infection was 27.6% in diabetes mellitus (both type-I and type-II), which was very high as compared to the general population

prevalence of hepatitis C infection<sup>2</sup>. Initially Ellison and co-workers reported that diabetes is more common in hepatitis C infection and the subsequent studies conducted worldwide, also supported this initial report<sup>16,17,18,19,20</sup>. While Simo Rafael pointed out first time that hepatitis C infection is more frequent in diabetes mellitus, which was again supported by various American and European studies<sup>21</sup>. If we compare our study with other studies then it shows similarity<sup>22,23</sup>. A very important data was analyzed from UKPDS trial which showed that hepatitis C was more prevalent in white Caucasian and Asian patients residing in Europe where prevalence is under 1%<sup>24</sup>. Hyperglycemia in people with chronic liver disease (hepatitis C) was attributed not only to insulin resistance but also to decreased insulin production<sup>25,26</sup>. But why hepatitis C infection is common in diabetes mellitus is still unknown.

Among many variables studied in our study, duration of diabetes, poor control of diabetes, insulin injection therapy, nephropathy, hypertension were significantly related with association with hepatitis C infection & diabetes mellitus longer.

Duration of diabetes mellitus was significantly related with hepatitis C infection may be due to the reason that these people are having decrease immunity and increased number of surgical interventions.

Uncontrolled diabetes mellitus was very significantly related with hepatitis C infection. Poorly controlled diabetes may predispose to hepatitis C infection and it is possible that HCV infection may serve as an additional risk factor for the development of diabetes, beyond that attributable to chronic liver disease alone<sup>27,28</sup>. Poor control of diabetes mellitus. Reasons may be due to insulin resistance, fibrosis of pancreas and fibrosis in liver<sup>29,30,31</sup>.

There is significant relation between insulin and hepatitis C infection suggesting sharing of needles among diabetics. Hypertension and nephropathy are also significantly related with hepatitis C infection. Either diabetic type-II nephropathy is having high frequency of hepatitis C infection or hypertension is caused by hepatitis C induced glomerulonephritis<sup>32,33,34</sup>.

### Conclusion:

Hepatitis C infection is common in diabetic patients as compared to general population. Out of diabetic patients HCV infection is more common with longer duration of diabetic mellitus, poor control of diabetic mellitus, hypertension, nephropathy and insulin therapy

Table 1

|                |             |
|----------------|-------------|
| Total patients | 250         |
| Male           | 120 (48%)   |
| Female         | 130 (52%)   |
| Type-I DM      | 06 (2.4%)   |
| Type-II DM     | 244 (97.6%) |

Table .2

| Age         | HCV +ve     | HCV -ve      |
|-------------|-------------|--------------|
| <30 years   | 06 (08.6%)  | 04 (02.20%)  |
| 30-39 years | 14 (20.28%) | 20 (11.04%)  |
| 40-49 years | 15 (21.73%) | 53 (29.28%)  |
| >50 years   | 34 (49.27%) | 104 (58.98%) |
| <b>BMI</b>  |             |              |
| <24.9       | 32 (46.37%) | 68 (37.56%)  |
| >25         | 37 (53.62%) | 113 (62.43%) |
| <b>Sex</b>  |             |              |
| Male        | 39 (56.5%)  | 81 (45%)     |
| Female      | 30 (43.5%)  | 100 (55%)    |
| <b>Area</b> |             |              |
| Rural       | 22 (31.88%) | 64 (35.35%)  |
| Urban       | 47 (68.12%) | 117 (64.64%) |

P value not significant

Table 3

| Duration of DM            | HCV +ve     | HCV -ve      | P -Value |
|---------------------------|-------------|--------------|----------|
| <one year                 | 14 (20.28%) | 80 (44.19%)  | <0.05    |
| 1-15 years                | 44 (63.76%) | 81 (44.75%)  |          |
| >15 years                 | 11 (15.94%) | 20 (11.04%)  |          |
| Uncontrolled DM           | 60 (87%)    | 75 (41.43%)  | <0.001   |
| Injection Insulin Therapy | 12 (17.39%) | 10 (5.52%)   | <0.005   |
| Nephropathy               | 65 (94.20%) | 146 (80.66)  | <0.01    |
| Hypertension              | 63 (91.30%) | 137 (75.69%) | <0.01    |

**References:**

- Doris B. Strader, Teresa Wright, David L. Thomas and Leonard B. Seeff. AASLD Practice Guideline. Diagnosis, Management and Treatment of Hepatitis C. 2004.
- 38<sup>th</sup> EASL, The European Association for the Study of Liver, 2003.
- Dr. Muhammad Umar, Dr. Bushra Khaar, Dr. Amir Rizwan. Rawalians Research Forum on G.I & Liver diseases. Practice Guidelines, Hepatitis (2003).
- National Institute of Health Consensus Development Conference Statement: Management of Hepatitis C: June 10-12, 2002 .Hepatology 2002;36:S1-S20 .
- Pakistan society of Gatrontology, Guidelines for management of Hepatitis B and hepatitis C, 2003.
- Gary L Davis; Schiff's diseases of the liver, eight edition, edited by Eugene R. Schiff, Michael F.Sorrel, Willis C. Maddrey, Lippincott-Raven Publishers, Philadelphia,1999.
- Shera AS, Rafique G, Khawaja IA, et al. Pakistan National Diabetes Survey prevalence of glucose intolerance and association factors in North West Frontier Province (NWFP) of Pakistan. J Pak Med Assoc 1999; 49: 206-11.
- ADA position statement (epidemiology of diabetes mellitus.) Diabetes Care, Vol 27, number 5, May 2004.
- Scheuer PJ, Ashrafzadeh P, Sherlock S, Brown D, Dusheiko G. The pathology of hepatitis C. Hepatology. 1992;15:567-71.
- Moriya K, Yotsuyanagi H, Shintani Y, Fujie H, Ishibashi K, Matsuura Y, et al . Hepatitis C virus core protein induces hepatic steatosis in transgenic mice. J Gen Virol. 1997;78:1527-31.
- Wong VS, Wight DG, Palmer CR, Alexander GJ. Fibrosis and other histological features in chronic hepatitis C virus infection: a statistical model. J Clin Pathol. 1996;49:465-9.
- Hourigan LF, Macdonald GA, Purdie D, Whitehall VH, Shorthouse C, Clouston A, et al. Fibrosis in chronic hepatitis C correlates

- significantly with body mass index and steatosis. Hepatology. 1999;29:1215-9.
- Wilson Charlton Hepatitis C infection and type 2 Diabetes in American-Indian women. Diabetes Care Sept, 2004.
- Qureshi H, Ahsan T, Mujeeb SA et al. Diabetes Mellitus is equally frequent in chronic HCV and HBV infection. J. Pak Med. Assoc. Jul, 2002;52(7):280-3.
- Mangia A, Schiavone G, Lezzi G. et al. HCV and diabetes mellitus: evidence for a negative association. Am. J. Gastroenterol. 1998 Dec;93(12):2363-7.
- Bilal Bin Younas, Gulsana Masood Khan, M. Akbar Chaudhary. Prevalence of Diabetes Mellitus among Patients suffering from Chronic Liver Disease. Mother & Child, Mar 2000;38(1):37-40.
- FraserGM, Harman I, Meller N, et al. Diabetes Mellitus is associated with chronic hepatitis C but not chronic hepatitis B infection. Isr J Sci 1996;32:526-530.
- Yang SQ, Chen HS, Jiang D et al. Relationship between chronic hepatitis C and type II diabetes mellitus. Zhonghua Shi Yan He Lin Chuang Bing Du Xue Zhi. 2003, Mar;17(1):46-9.
- Brischetto R, Como C, Amore MG. Prevalence and significance of type-2 diabetes mellitus in chronic liver disease, correlated with hepatitis C virus. Ann Ital Med. Int. 2003 Jan-Mar;18(1):31-6.
- Thuluvath PJ, John PR. Association between hepatitis C, diabetes mellitus, and race. A case-control study. Am. J. Gastroenterol. 2003 Feb;98(2):438-41.
- Rafael Sim, Cristina Hern, Joan Genesc et al. High Prevalence of Hepatitis C Virus Infection in Diabetic Patients. Diabetes Care Volume 19, Number 9, September 1996, Page 998.
- Murphy EL, Bryzman S, Williams AE. Et al. Demographic determinants of hepatitis C virus seroprevalence among blood donors. JAMA. 1996 Apr 3;275(13):995-1000.
- Graeme J.M. Alexander, MA, MD, FRCP. An Association between Hepatitis C Virus Infection and Type 2 Diabetes Mellitus: What Is the Connection?(Editorial). 17 Oct 2000 , Vol 133(8):( 650-652
- Gray H, Wrehgitt T, Stratton IM et al. High prevalence of hepatitis C infection in Afro-Caribbean patients with type-2 diabetes and abnormal liver function tests. Diabet Med. 1995 Mar;12(3):244-9.
- Gunsar, US Akarca et al. Diabetes mellitus, insulin resistance and hypocoatabolism in chronic HCV infection. American Association for the Study of Liver Diseases – 1996 Annual Meeting.
- Jason M Hui. Insulin resistance is associated with chronic hepatitis C and virus infection fibrosis progression. Gastroenterology. Volume 125, Number 6, Dec 2003.
- Takumi Kawaguchi , Takafumi Yoshida , Masaru Harada , et al. Hepatitis C Virus Down-Regulates Insulin Receptor Substrates 1 and 2 through Up-Regulation of Suppressor of Cytokine Signaling 3. American Journal of Pathology. 2004; 165: 1499-1508.
- Albert Lecube, PHD , Cristina Hernandez, MD, Joan Genesea, MD, et al. High prevalence of Glucose Abnormalities in Patients with Hepatitis C Virus Infection. Diabetes Care. 27: 1171-1175, 2004.
- Nasir Khokhar Association of Chronic Hepatitis C Virus Infection and Diabetes Mellitus Pakistan J. Med. Res. 04, 2002, Vol. 4, 1-6
- Ali H. Mokdad, PhD et al. Increases in obesity and diabetes among US adults continue in both sexes, all ages, all races, all educational levels, and all smoking levels. JAMA. 2003;289:76-79.
- J. Soma et al .High Prevalence and Adverse Effect of Hepatitis C Virus Infection in Type II Diabetic-Related Nephropathy. J.Am.Soc.Nephrol..April 1, 2000;11(4):690-699.
- Abdourakhmanov DT, Hasaev AS et al. Epidemiological and clinical aspects of hepatitis C virus infection in the Russian Republic of Daghestan. Eur J Epidemiol. 1998 Sep;14(6):549-53
- Chronic hepatitis C and type II diabetes mellitus: a prospective cross-sectional study. Zein CO; Levy C; Basu A; Zein NN Am J Gastroenterol 2005 Jan;100(1):48-55.