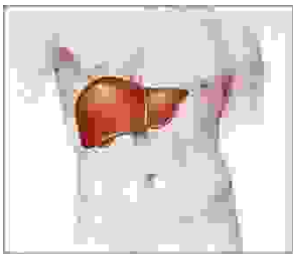
ORIGINAL PROF-804

RELATIONSHIP BETWEEN CHRONIC HEPATITIS C AND TYPE-2 DIABETES MELLITUS IN BHAWALPURIAN PATIENTS



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ABSTRACT... imran_suliman@yahoo.co.uk **Objective:** To establish a potential relationship between chronic hepatitis C virus infection and diabetes mellitus in Bahawalpur **Design:** Comparative study. **Setting & period:** Bahawal Victoria Hospital and four different private clinics in Bahawalpur during 2002 to 2003.**Material &Methods:** 1. The case record files of 100 patients with chronic hepatitis C vs. 100 with chronic hepatitis B were reviewed and the laboratory and demographic data were extracted. 2. Anti-HCV and HBsAg were determined for 100 type 2 diabetes patients and 100 healthy adults by ELISA. The diagnosis of diabetes was based on the new WHO criteria. Pearson's correlation coefficient was calculated and tested for significance. **Results:** 1. The occurrence of diabetes in patients with chronic hepatitis C was 19%, higher than 8% in patients with chronic hepatitis B ($P<0.01$). Age and HCV infection were independent risk factors for diabetes. 2. Three patients with type 2 diabetes were anti-HCV positive while none of the 100 healthy adults was anti-HCV positive ($P<0.05$). Four patients with diabetes and five healthy adults were HBsAg positive ($P>0.05$). **Conclusion:** 1. Diabetes Mellitus was found to be significantly more frequent among HCV related liver disease patients when compared with HBV infected liver patients. 2. The frequency of anti HCV was higher in diabetes patients as compared to healthy adults. HCV can be a trigger factor in the development of diabetes mellitus.

Key words: Diabetes Mellitus, HbsAg, anti HCV, ELISA

INTRODUCTION

Patients with liver disease are known to have a higher prevalence of glucose intolerance, preliminary studies suggest that hepatitis C virus (HCV) infection may be an additional risk factor for the development of diabetes mellitus.[1]The first evidence for an association between hepatitis C virus(HCV) infection and diabetes mellitus emerged in published form in 1994.[2] Since then a lot of research has been done to verify the link between hepatitis C virus infection and

diabetes mellitus.[3] Later on the data revealed type 2 diabetes to be more prevalent among patients with chronic hepatitis C infection[4,5]. Further reports discovered that HCV infected patients beyond middle age were more prone to develop diabetes mellitus regardless of having cirrhosis of liver[6]. Others claimed that the prevalence of diabetes mellitus was associated closely with the Child-Pugh score.[5] Mangia and associates and many others' findings disprove HCV infection as a trigger factor for DM, which should not be listed among the various extra hepatic manifestations of this viral infection[7].Impaired glucose tolerance frequently occurs in patients with chronic liver disease. Hyperinsulinaemia and peripheral insulin resistance contribute to the development of DM in these patients[8].

It could be suggested that type 2 diabetes mellitus in patients with HCV-related chronic liver disease be facilitated by hepatic iron overload and mitochondrial damage[9].

Fasting insulin levels in patients with HCV-related cirrhosis and diabetes mellitus were found to be elevated significantly, consistent with insulin resistance. However, acute insulin responsiveness was reduced in patients with HCV infection and diabetes suggesting concomitant β-cell dysfunction[5].

The objective behind the study was to investigate any link between HCV infection with diabetes mellitus in our population.

MATERIALS & METHODS

This comparative study including 300 patients and 100 healthy populations was carried out in Bahawal Victoria Hospital and four different private clinics in Bahawalpur during 2002 to 2003. The case record files of 100 (50 males and 50 females) patients with chronic hepatitis C vs. 100(50 males and 50 females) with chronic hepatitis B were reviewed randomly and the laboratory and demographic data including age, sex, address, body mass index, alcohol consumption, marital status, extra marital affairs, frequent needle syringe injections, smoking, any addictions, family history of diabetes mellitus were extracted. The diagnosis of diabetes mellitus was made as according to new WHO criteria.[10] Duration of the diagnosis and treatment of diabetes mellitus before anti HCV or HBsAg positivity through ELISA was also noted.

Anti-HCV and HBsAg were determined for 100 (50 males and fifty females) enrolled type 2 diabetes patients and 100(fifty males and fifty females) healthy adults by ELISA after getting informed consent. Those who were under treatment for diabetes mellitus were categorized as diabetic. Serum glucose determination was done in others and was categorized as diabetic if fasting glucose levels exceeded 126mg/dl on more than one occasion, in absence of specialized diet or parenteral nutrition. None of them had history of previous icterus or other signs of hepatitis, received blood transfusions, or were on hemodialysis.

The categorical variables of the numerical data were evaluated by applying student t test. Pearson's correlation coefficient was calculated and tested for significance.

RESULTS

Nineteen patients who were positive for anti HCV through ELISA were found to be diabetic (19%). Interestingly all were urban and fifteen of them were females. The age ranged from 32 to 74 years (Mean53). Average height was 160.23 cm and average weight was 64.77±11.22 kg. The onset of diabetes mellitus before the diagnosis of positive anti HCV varied from one to eight years (Mean 3.2years). Three were on oral hypoglycemic agents, sixteen were taking insulin injections. All were married and three disclosed their extra marital sexual histories. None of them was alcoholic addict or smoker. Six were having positive family history of diabetes mellitus. There was positive history of needle syringe injections in all of them.

Eight patients who were positive for HBsAg through ELISA were having diabetes mellitus (8%). Five of them were urban (3 females and 2 males) and three (all males) belonged to rural areas. The age ranged

from 28 to 72 years (Mean 50). Average height was 69.34 cm and average weight was 64.67 kg. The onset of diabetes mellitus before the diagnosis of positive HBsAg varied from two to ten years (Mean5.4 years). Six were married and none of them gave history of extra marital sexual relationships. None of them was alcoholic or addict .Two were smokers. All said yes to the question about family history of diabetes mellitus and needle syringe injections in the past. Two of them were on oral hypoglycemic agents and six were receiving insulin therapy.

Three patients with type 2 diabetes were anti-HCV positive while none of the 100 healthy adults was anti-HCV positive (P<0.05). All were urban and females. Their ages ranged from 44 to 56 years (Mean 50 yrs). Average height was 67.34 cm and average weight was 62.67 kg. The duration of diabetes mellitus varied from three months to three years (Mean1.1years). All were married and none of them gave history of extra marital sexual relationships. None of them was alcoholic, addict or smoker. History of needle syringe injections and positive family history of diabetes mellitus were present in all. All were on oral hypoglycemic agents.

Four patients with diabetes were HBsAg positive; one was rural and the other three were city dwellers. Three were males. Their ages ranged from 48 to 61 years (Mean 54.5). Average height was 69.23 cm and average weight was 60.36 kg. The duration of diabetes mellitus varied from one year to seven years (Mean three years). All were married and one of them gave history of extra marital sexual relationships. One of them was alcoholic as well as smoker. History of needle syringe injections and positive family history were positive in all three and all were on oral hypoglycemic agents.

Five healthy adults were HBsAg positive, four were pregnant females and one was male; all of urban origin with age ranged from 29 to 44 years (Mean36.5) and average weight was72.45kg and average height of 60.01 cm. History of needle syringe injections was positive in three of them.

DISCUSSION

Ninety four percent of our anti HCV patients found to be diabetic were above forty years of age. These figures are exactly similar to a study conducted in Saudi Arabia (KSA)[11] and another in Korea.[12] Sixty three percent of HBsAg positive who were found to be diabetic were above age forty while the figures of KSA was 76%(p>0.05). Less number of patients in our study were having family history of diabetes mellitus when compared with the study of KSA.

Table-I. Frequency of Diabetes Mellitus

Studies	Anti HCV Positive pts (%)	HBsAg positive pts (%)
Our study	19	8
Islamabad[20]	18*	-
Karachi[14]	24.5**	19.4**
KSA[11]	21.2*	14.1**
Egypt[18]	25**	-
Israel[6]	33**	12*
Korea[12]	24**	10.4*
Korea[8]	22*	-
China[13]	19.05*	8.37*
Italy [21]	18.96*	1.46**
Italy [21]	32.5**	6.6*
Sicily[5]	24.4**	7.9*
Los Angles[1]	21*	12*

*p>0.05 **p <0.05

The occurrence of diabetes in patients with chronic hepatitis C was 19%, higher than 8% in patients with chronic hepatitis B (P<0.01).The results correlate with another study conducted in China[13] 19.05% and 8.37% respectively(p>0.05) but the results at Karachi[14] were 24.5% and 19.4% (p<0.05).The comparison with other local ,Indian, Far Eastern, Mid Eastern, European and American studies are given in Table-I. Mangia[7] provided evidence to prove a negative association between HCV and diabetes mellitus in his Italian patients.

Three patients with type 2 diabetes were anti-HCV positive while none of the 100 healthy adults was anti-HCV positive (P>0.05).Again the results are similar to the study in China[13] where the figure were 3.12% and zero (p>0.05).Qureshi[14] found 5.1%incidence of anti HCV in his diabetic population (p<0.05) and 4.3% in healthy controls (p<0.05).

Four patients with diabetes and five healthy adults were HBsAg positive .These results are similar to the results of Ryu JK[12] in Korean population (4.5%) and Yang SQ[13] (4.37% and 5.38% respectively) (p>.05). Atabek[15] found no difference in serological evidence of HCV and HBV in diabetics and healthy Turkish peoples as controls but his study population consisted of type 1 diabetics. Comparison with other studies is given below in Table II.

Table-II. Frequency of positive anti HCV & HBsAg

Studies	Frequency of +ve anti HCV in		Frequency of +ve HBs Ag in	
	Diabetes mellitus (%)	Healthy controls (%)	Diabetes mellitus (%)	Healthy controls (%)
Our study	3	-	4.0	5.0
Karachi[14]	5.1*	4.3**	-	4.9*
Turkey[22]	7.5*	0.1*	0.1**	5.1*
Korea[12]	2.1*	-	4.5*	-
China[13]	3.12*	-	4.37*	5.38*
United states[1]	4.2*	1.6*	-	-
India	13.2**	-	17**	-

*p >0.05, **p<0.05

Considering the figures in our study prevalence of diabetes mellitus in chronic hepatitis C virus infection seems to be high. Some believe it to be increasing fibrosis in these patients[16], others believe it a result of direct destruction of pancreatic cells[17], considering the presence of islet cell antibodies in 44.4% of patients of hepatitis C in one study[18]. Many others noted deposition of fat in liver cells leading to insulin resistance among HCV core protein expressers which may lead to type2 diabetes mellitus[19]. It could be suggested that type 2 diabetes mellitus in patients with HCV-related chronic liver disease could be facilitated by hepatic iron overload and mitochondrial damage.[9]

CONCLUSION

Diabetes mellitus is significantly more common in patients with HCV related liver disease than in patients with HBV related liver disease. Moreover the occurrence of anti HCV is higher in diabetic patients than in healthy adults that allow us to define it as a group at risk for viral hepatitis. HCV may play a role in the development of type 2 diabetes mellitus.

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