Original Article

Risk of Type II Diabetes in Viral Hepatitis B and C Patients

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ABSTRACT

OBJECTIVE: To find out the prevalence of type II diabetes in viral hepatitis B and C patients of different age groups with and without cirrhosis.

METHODS: This observational study was carried out in the Department of Biochemistry, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Center Karachi, during the period June 2007 to June 2008. Eighty hepatitis B and C virus infection positive patients with and without cirrhosis were selected for study after confirmation of their diagnosis by ELISA method. Normal subjects were selected as controls for study. Blood glucose was estimated by Hexokinase method, while enzymes assay was done by enzymatic (kinetic) method. Data analysis including paired and correlation analysis were carried out and P value upto 0.05 was considered significant.

RESULTS: The number of diabetic patients was high (55%) in age group 40-49. Patients with cirrhosis of hepatitis C were having high risk (40%) than of hepatitis B (23%) of developing diabetes. This trend was also observed in patients of without cirrhosis (27% hepatitis C, 10% hepatitis B). Increasing fasting blood glucose level associated with increase in hepatic enzymes (AST and ALT) levels was observed. It was an indicator of ongoing liver damage in co-morbid condition of viral hepatitis.

CONCLUSION: In addition to the derangement of liver function, patients of viral hepatitis B and C can be at the risk of development of type II diabetes. Earlier measures are needed for the prevention of the disease at earlier stage of development.

KEY WORDS: Type II diabetes, insulin resistance, cirrhosis, viral hepatitis B and C, ELISA.

INTRODUCTION

Viral hepatitis is an infection of hepatocytes that produces necrosis and inflammation of the hepatic tissue.[1] Among different viruses, hepatitis B and C are the most common causes of chronic liver disease and cirrhosis worldwide. Patients with dual HBV and HCV infections have more severe liver disease and are at an increased risk for progression to hepatocellular carcinoma.[2,3] In endemic areas, majority of the individuals are infected by vertical transmission in the early childhood.[4] Most infections of hepatitis B and C viruses are caused from unsafe injection practices. These may also occur due to medical, surgical or dental treatment and by vertical transmission from mother to child.[5] Multiple sexual partners is the most commonly reported factor for patients with acute hepatitis B. Other factors associated with patient-to-patient transmission include multidose vials, finger-stick devices, acupuncture needles and jet injection guns.[6]

The hepatitis B virus (HBV) and hepatitis C virus (HCV) are noncytopathic, hepatotropic members of the hepadnavirus and flavivirus families respectively and cause acute and chronic necro inflammatory hepatic disease and hepatocellular carcinoma.[7] The inflammatory process in liver is progressive and lead to cirrhosis in 20-50% of patients after 10-20 years.[8] In addition to liver disease, viral hepatitis infection is associated with changes in cognitive and psychiatric functions, a decreased quality of life and an increased prevalence of diabetes mellitus[9]. In chronic infection, it is associated with glucose intolerance.[10]

Diabetes mellitus is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin. It occurs most often either due to autoimmune type 1 or to adult onset type II diabetes.[11] Chronic viral hepatitis is associated with the increased risk of development of type II diabetes mellitus due to impaired glucose metabolism.[12] However, no single mechanism can explain the link between hepatitis virus infection and type II diabetes mellitus. The fatty degeneration and cirrhosis have been associated with abnormal glucose regulation. The fatty change is related to intracellular fat accumulation and insulin resistance.[13] The virus core protein inhibit secretion of very low density lipoprotein in the hepatic tissue and consequently induces fatty degeneration.[14] Hepatitis virus is also able to trigger autoimmune mechanism against the insulin producing pancreatic beta cells in susceptible individuals. Other factors, such as obesity characterized by high body mass index, advanced age and family history of diabetes are associated with the higher prevalence of diabetes in the viral hepatitis infected population.[16]

The present study was designed to find out the prevalence of type II diabetes in viral hepatitis B and C patients of different age groups with and without cirrhosis.

SUBJECTS AND METHODS

This was an observational study carried out in the Department of Biochemistry, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Center Karachi, during the period June 2007 to June 2008. Patients were selected for the study with the collaboration of Liver Clinic, medical wards and PMRC, JPMC, Karachi. Finally 80 patients of both genders with an established diagnosis of hepatitis B and C and with and without cirrhosis were recruited. Patients were divided into different groups according to cause and type of their disease: group I, hepatitis B patients without cirrhosis; group II, hepatitis C patients without cirrhosis; group III, hepatitis B patients with cirrhosis and group IV, hepatitis C patients with cirrhosis. (Patients whose case history showed a concomitant presentation with the conditions like prior anti-viral treatment, pregnancy, a body-mass index > 25, family history of diabetes, and with any other associated chronic illness were excluded from the study. Similarly patients with hepatitis B and C virus co-infection were also excluded from the study.) For comparative analysis, a control group of 20 normal subjects matched for age and gender were also enrolled in the study.

Six ml of venous blood was collected from the superficial vein of each subject with the help of disposable syringe under all aseptic measures and aliquoted in plain test tubes without anticoagulant; 1.8 ml blood was transferred into a tube containing 0.2 ml citrate for prothrombin time, while remaining blood after clotting was centrifuged to obtain serum. After that serum was labeled and stored at -70ºC in freezer for later analysis.

The estimations of fasting blood glucose was done by Hexokinase method (DiaSys, Germany), hepatic enzymes (AST and ALT) by enzymatic (Kinetic) method (Merck, Germany) and serum albumin by Monochromator (End Point) method (Merck, Germany) by using analyzer of Slectra Junior of Vital Scientific (Netherland), while prothrombin time was analyzed by one stage (coagulation) method (Bio Merieux, France) using Hemaclot Human (Germany) Analyzer.

Statistical Analysis:

Data analysis including paired and correlation analysis were carried out by using SPSS version 10.0 for windows. Paired sample t-test was used to determine the significance of changes in quantitative parameters. P value of 0.05 or less was considered to indicate statistical significance.

RESULTS

The number of diabetic cases present in different groups were, in group I: 2 (10%), group II: 5 (23%), group III: 6 (27%) and in group IV: 9 (40%). The mean age of patients was 39 years with a range of 20-59 years. The age wise prevalence of diabetes was 1 (4%) in 20-29 years age group while 5 (23%) in 30-39 years, 12 (55%) in 40-49 years and 4 (18%) in 50-59 years age groups respectively. Therefore patients of hepatitis B and C with cirrhosis were greater having diabetes and also majority of patients were of older (30-49 years) group **(Table I)**.

The mean values of age, fasting blood glucose and prothrombin time were statistically significant ($P<0.05$) in groups III and IV as compared to control. Whereas mean values of AST and ALT were statistically highly significant in all groups. However albumin showed statistically significant mean values in all groups as compared to control **(Table II)**. The fasting blood glucose in all groups showed significant ($P<0.01$) positive correlation with prothrombin time, AST and ALT, while negative correlation with albumin **(Table III)**. Thus high fasting blood glucose level in patients with cirrhosis concomitant with ongoing liver damage was an indicator of development of co-morbid condition in these patients.

TABLE I: DISTRIBUTION OF DIABETICS IN DIFFERENT GROUPS AND BY AGE

Groups	No: of Subjects	No: of Diabetics Subjects	Age Group			
			20-29	30-39	40-49	50-59
Group I	20	2 (10%)	0	1	1	0
Group II	20	5 (23%)	1	1	2	1
Group III	20	6 (27%)	0	1	4	1
Group IV	20	9 (40%)	0	2	5	2
Total	80	22 (17.6%)	1 (4%)	5 (23%)	12 (55%)	4(18%)

Criteria of DM = Fasting Blood Glucose > 110 mg/dl and Insulin > 9 µU/ml

Group I: Hepatitis B patients without cirrhosis. Group II: Hepatitis C patients without cirrhosis.

Group III: Hepatitis B patients with cirrhosis. Group IV: Hepatitis C patients with cirrhosis.

TABLE II: COMPARISON OF BIOCHEMICAL PARAMETERS BETWEEN DIFFERENT GROUPS

Parameter	Control (n=20)	Group I (n=20)	Group II (n=20)	GroupIII (n=20)	Group IV (n=20)
Age (Years)	36.4±1.93	36.4±1.93	36.4±1.93	41.9±1.39*	41.9±1.42*
Fasting Blood Glucose(mg/dl)	88±3.40	89±3.60	94±4.80	117±10.87*	134±15.85*
Prothrombin time (Control: 11 to 16 sec)	13.7±0.38	17.2±1.02	16.1±0.69	19.4±1.28*	19.6±0.95*
AST (U/L)	15.2±1.08	76.6±7.36**	72.9±5.95**	123.7±17.41***	128.2±15.65***
ALT (U/L)	27.4±1.25	81.6±7.94**	79.4±5.90**	95.6±10.42**	87.1±10.65**
Albumin (g/dl)	4.66±0.14	3.86±0.11*	3.56±0.15*	2.87±0.08**	2.88±0.06**

Individual values are expressed as mean ± SEM.
* P<0.05, ** P<0.01, *** P<0.001.

TABLE III: CORRELATION COEFFICIENT (R) BETWEEN FASTING BLOOD GLUCOSE AND VARIOUS BIOCHEMICAL PARAMETERS OF VIRAL HEPATITIS

Parameter	Group I (n=20)	Group II (n=20)	Group III (n=20)	GroupIV (n=20)
Prothrombin time	0.91*	0.77*	0.80*	0.46*
AST (U/L)	0.97*	0.95*	0.91*	0.91*
ALT (U/L)	0.96*	0.91*	0.86*	0.50*
Albumin (g/dl)	-0.82*	-0.41	-0.62*	-0.44

* P<0.05

DISCUSSION

Viral hepatitis exists throughout the world and is a major global health problem. Hepatitis B, C and D viruses cause persistent and chronic infection. Hepatitis B and C viruses involve liver and also produce extrahepatic manifestations. Type II diabetes mellitus is one of the complications of the disease. It is a co-morbid condition of chronic liver disease and biochemical evidence of ongoing liver damage may be detected in a large proportion of diabetic patients.[15] Custro *et al*.[16] reported that the incidence of diabetes mellitus in adults with chronic hepatitis B and C is four times higher than that in general population. As the disease progresses, the risk of developing type 2 diabetes is increased due to development of resistance to the action of insulin, which ultimately leads to increased blood glucose level (hyperglycemia).

Because age is an important risk factor for type 2 diabetes, Papatheodoridis *et al*[15] and Wang *et al*[17] analyzed the relation of viral hepatitis infection and type 2 diabetes according to different age groups, and found age as an important risk factor for type 2 diabetes in both hepatitis B and C virus infected cases and its association with older age. They also observed that the risk of diabetes was not much different in those ≥ 60 years of age, perhaps because of the fact that those patients, who have both viral infection and diabetes mellitus, are more likely to die of advanced liver disease. In our study also majority of the diabetic cases were of older age group.

In present study we observed that the number of diabetic patients with cirrhosis were twice (33.5%) than that without cirrhosis (16.5%). This reflects the need for diagnosis of diabetes at the earlier stage of acquiring hepatitis, because diabetes itself increases the rate of progression of fibrosis. These findings match with the study of Mason *et al*[18], who also observed the increasing number of diabetic patients with increase in severity of disease.

In the studies of Papatheodoridis *et al*[15] and Qureshi *et al*[19], more number of hepatitis C virus infected cases were observed as diabetic than hepatitis B virus infected cases. We also observed the more number of diabetic cases (35%) in hepatitis C virus induced patients with and without cirrhosis, as compared to hepatitis B virus induced patients (20%). It probably reveals the effect of causative organism on the development of diabetes.

Biochemical analysis revealed that fasting blood glucose levels were associated with higher levels of AST and ALT, along with derangement of other biochemical parameters, which indicates ongoing liver damage associated with the development of type II diabetes. These observations are in accordance with the study of Alizadeh *et al*[12], Wang *et al*[20] and Papatheodoridis *et al*[15] who observed the development of diabetes in association with liver function deterioration in hepatitis B and C infected patients.

CONCLUSION AND RECOMMENDATIONS

The patients of chronic viral hepatitis B and C and cirrhosis, with the advancement of disease, can be at the risk of development of type II diabetes, in addition to the derangement of liver function.
Further studies at mass level are highly suggested to highlight the risk and to suggest the measures needed for the prevention of the disease at earlier stage of development.

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