

THE PREVALENCE OF HEPATITIS B AND HEPATITIS C VIRUS IN DIABETIC PATIENTS

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ABSTRACT

Objective: Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are important health problems throughout the world. These virus infections can cause chronic hepatitis, cirrhosis or hepatocellular carcinoma. The association of diabetes mellitus with liver disease was recognized many years ago and it has been documented in numerous studies. This association might be related to diabetes mellitus causing chronic liver disease or vice versa. It was reported that diabetes mellitus seems to be more frequent in chronic hepatitis C cases and patients who have type II diabetes mellitus have higher antiHCV seropositivity than normal. For this reason, frequency of HBsAg, antiHBs, antiHCV and its relation to the duration of diabetes, age of patients, and type of antidiabetics used was evaluated among our hospital diabetic outpatient clinic patients in the present study.

Methods: Seventy-four type I and II diabetic patients followed by Haydarpaşa Numune Education and Research Hospital Diabetic's

outpatient clinic between October 1999 and March 2000, participated in this study. The 3rd generation ELISA method was used for hepatitis markers detection with the " The Organon Technica " kits.

Results: According to our study results, the frequency of HBsAg, antiHBs, antiHCV was found to be 4 %, 29 %, 4 % respectively among our study group. It was seen that antiHCV seropositivity in diabetic patients is higher than normal population. There is no statistical relationship between the hepatitis B and C markers positivity and age, duration of diabetes mellitus and type of antidiabetics used.

Conclusion: As a result HBV incidence is similar to the normal population whereas HCV infection incidence is higher among diabetics than in the normal population. However to clarify the incidence of HCV infection among diabetic patients, we need further confirmative studies.

Key Words: HBV, HCV, Diabetes mellitus.

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INTRODUCTION

Viral hepatitis is one of the most common infections. The known causative agents are hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis delta virus (HDV), hepatitis E virus (HEV) and newer hepatitis virus such as hepatitis F virus (HFV), hepatitis G virus (HGV) and transfusion - transmissible virus (TTV). The viral hepatitis can be acute or chronic. Chronic hepatitis is mostly caused by HBV, HCV, HDV. Chronic hepatitis is a well known risk factor for cirrhosis and hepatocellular carcinoma (1-4).

Hepatitis B virus infection is one of the most important health problems in the world. It was reported that more than two billion people are confronted with HBV. Hepatitis C virus infection is also an important health problem throughout the world as HBV infection. These virus infections can cause chronic hepatitis, cirrhosis, and hepatocellular carcinoma. The host immunity is very important in progressive cases (3,4).

Diabetes mellitus is one of the most common endocrine diseases. The diabetes mellitus incidence is 1-2 % according to the fasting hyperglycemia. The disease is characterized by metabolic abnormalities and long term complications. The effect of diabetes mellitus on the immune system, and the association of diabetes mellitus with chronic liver disease is shown in many studies (5,6). The diabetes mellitus incidence is high especially in patients with chronic HCV infection and anti HCV positivity is reported more frequently in type II diabetic patients than in the normal population (7). AntiHBs positivity was found to be high in some previous studies, probably due to inappropriate use of the insulin syringe. In recent years this incidence decreased with improved hygienic conditions (8-10). In this study the frequency of HBsAg, antiHBs, antiHCV and its relation to the duration of diabetes, and type of antidiabetics used was evaluated among our hospital diabetic outpatient clinic patients.

MATERIAL AND METHOD

Seventy-four type I and II diabetic patients were followed by Haydarpaşa Numune Education and

Research Hospital Diabetic's outpatient clinic between October 1999 and March 2000, participated in this study. All patients were questioned about the antidiabetic medications (oral, insulin) they used, how long they had known that they were diabetic, how long they had been using antidiabetics, whether they had had any operation previously, whether they had had any blood or blood products transfusions, whether they had had hepatitis before. We collected the serum of patients to assess antiHCV, HBsAg, antiHBs, antiHBc total status with biochemical parameters. The 3rd generation ELISA method was used for hepatitis markers detection with the "The Organon Technica" kits. The statistical analysis was done via Student's t test, Fisher's exact test and Pearson's correlation analysis test. One sample Student's t test was used for comparing HBsAg and antiHCV positivity between diabetics and Turkey average. Fisher's exact test was used to coanalyse antiHBc status and type of used antidiabetic. The relationship between antiHBc status and the duration of diabetes mellitus was analysed by Pearson's correlation analysis test. The relationship between antiHBc status and age in diabetics was analysed by Pearson's correlation analysis test.

RESULTS

Forty nine of 74 diabetic patients were female and 25 were male. Twenty three of the patients were using insulin, 48 of 74 patients were taking oral antidiabetics. Three patients had had on antidiabetic regime. The mean age of the diabetics was 54.98.

Forty two of 74 patients (56.7 %) had negative hepatitis markers against HBV. Two patients (2.7 %) were only antiHBs positive, 5 patients (6.8 %) were only antiHBcIgG positive, 22 patients (29.8 %) were antiHBs and antiHBcIgG positive, 3 patients (4 %) were HBsAg and antiHBcIgG positive, 3 patients (4 %) were antiHCV positive and one of them was HBsAg and antiHBcIgG positive (Table I). One patient had both chronic HBV and HCV infection. The other had antiHCV positive. According to our study HBs Ag positivity is found in the normal range due to Turkey average values. AntiHCV positivity is over the Turkey average (Table II, $p < 0.05$).

Table I: The distribution of hepatitis markers among 74 diabetic patients

| | n | (%) |
|---------------------------------------|----|------|
| HBsAg and antiHBcIgG positivity (n) | 3 | 4.0 |
| antiHBs and antiHBcIgG positivity (n) | 22 | 29.7 |
| antiHBcIgG positivity (n) | 5 | 6.8 |
| antiHBs positivity (n) | 2 | 2.7* |
| antiHCV positivity (n) | 3 | 4.0 |
| * Vaccinated | | |

Table II: The comparison of HBsAg and antiHCV positivity between diabetic patients and Turkey average

| | antiHCV (+) | HBsAg (+) |
|--|---------------|------------|
| Diabetic patients (%) | 4% | 4% |
| Turkey average* | 0.6% (0.2-1%) | 5% (4-11%) |
| t= 41.991 (one sample Student's t test), p = 0.0006 (p<0.05) | | |
| * (1,19) | | |

We investigated whether there is any relation between oral antidiabetics or insulin use and the HBsAg, antiHBcIgG, antiHBs, antiHCV positivity. Our study results show that there is no relation between hepatitis B virus frequency and the type of antidiabetics used (Table III, p>0.05). All three antiHCV positive patients were using insulin.

We also tried to assess the relation between the duration of diabetes mellitus or age and HBsAg, antiHBcIgG, antiHBs, antiHCV positivity. According to our study results there is no relation between hepatitis B frequency and the duration of diabetes mellitus or age (Table IV, Table V, p>0.05). The duration of diabetes mellitus in anti HCV positive patients was 15 years, 1.5 years, 6 years. AntiHCV positive patients were 49,58,22 years old respectively.

Table III: The distribution of hepatitis B markers among insulin, oral antidiabetic user and antidiabetic diet taking patients.

| | HBsAg (+) and antiHBcIgG (+) | antiHBs (+) and antiHBcIgG (+) | antiHBcIgG (+) | Total (n) |
|---|------------------------------|--------------------------------|----------------|-----------|
| Insulin | 1 | 7 | 0 | 8 |
| Oral antidiabetic | 2 | 12 | 5 | 19 |
| Antidiabetic diet | 0 | 3 | 0 | 3 |
| Total (n) | 3 | 22 | 5 | 30 |
| p= 0.7967 (Fisher's exact test), Odds ratio: 0,8140 | | | | |

Table IV: The distribution of antiHBcIgG positivity and negativity with the duration of diabetes mellitus

| Duration of diabetes mellitus | antiHBcIgG (+) | antiHBcIgG (-) | Total (n) |
|-------------------------------|----------------|----------------|-----------|
| 0-5 year | 6 | 16 | 22 |
| 6-10 year | 11 | 12 | 23 |
| 11-15 year | 3 | 7 | 10 |
| 16-20 year | 4 | 4 | 8 |
| 21 and upper year | 6 | 5 | 11 |
| Total (n) | 30 | 44 | 74 |

r= 0.4960 (Pearson's correlation analysis test),
The two-tailed p value is 0.3954.

Table V: The distribution of antiHBcIgG positivity and negativity with age of diabetics

| Period | antiHBcIgG (+) | antiHBcIgG (-) | Total (n) |
|--------------|----------------|----------------|-----------|
| 15-24 | 0 | 1 | 1 |
| 24-34 | 0 | 1 | 1 |
| 35-44 | 2 | 2 | 4 |
| 45-54 | 8 | 18 | 26 |
| 55-64 | 9 | 17 | 26 |
| 65 and upper | 11 | 5 | 16 |
| Total (n) | 30 | 44 | 74 |

t = 0.4797 (Pearson's correlation analysis test),
The two-tailed p value is 0.1272.

DISCUSSION

Diabetes mellitus and chronic liver disease association have been implicated for many years. Initially diabetes mellitus can cause direct liver damage. Nuclear and cytoplasmic glycogen accumulation, lipid deposition and perisinoidal fibrosis are commonly seen in diabetics. And there are some reports that cirrhosis is one of the infrequent complications of diabetes mellitus. In recent years, it was shown that diabetes mellitus can cause nonalcoholic hepatosteatosis or cirrhosis. The prevalence of diabetes mellitus and cirrhosis has wide variations. Similarly chronic liver disease could also cause diabetes mellitus. More than 70 % of cirrhotics have abnormal oral glucose tolerance test (OGTT). There may be hyperinsulinism and insulin resistance (5,6).

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are important health problems

throughout the world. These virus infections can cause chronic hepatitis, cirrhosis or hepatocellular carcinoma. The diabetes mellitus incidence is high especially in patients with chronic HCV infection and antiHCV positivity is reported more frequently in type II diabetics than normal population. There are many studies related to incidence of HBV and HCV infection in diabetics that support increased frequency of HCV infection. But these studies are not systematically designed. The HBV or HCV infection incidence among diabetics has been found more frequently than normal population in various studies. This increased frequency might be associated with frequent parenteral applications or prolonged hospitalization in these patients. In recent years authors concluded that chronic HCV infection incidence was higher than HBV infection in diabetics. And they also had found that HCV incidence was higher than HBV infection in diabetics. And they also had found that HCV incidence was higher in diabetics than in the controls (4,7,11-15). Özyılkan et al (16) found 8% antiHCV positivity which was higher than in the normal population. Frasser et al (15) found that antiHCV positivity was higher in diabetics than in the normal population and that HBV incidence was close to that in the normal population. Balık et al (17) also found 6% antiHCV positivity and 5% HBsAg positivity. Another study from Bederida and et al (18) among 2465 diabetics concluded that HBsAg positivity was less than in the controls (3.5% and 6.9% respectively). They found high antiHCV incidence among diabetic patients that may be associated with T cell response resistance. According to our study results the HBsAg positivity is 4 % ($p>0.05$), antiHBs positivity is 29% ($p>0.05$), antiHCV positivity is 4% ($p>0.05$). The only antiHBcIgG positivity is 6.8% and the liver function tests of these patients are normal, this condition can be probably due to deficient immunity. We concluded that HBV frequency was not more than in the normal population among our outpatient diabetic clinics patients, and HCV positivity with 4 % was clearly more than in the normal population. This result correlates with other studies.

It was documented with various investigations whether there was any relationship between oral antidiabetics or insulin use and the HBsAg, antiHBcIgG, antiHBs, antiHCV positivity. The

HBsAg positivity was 6.9% among insulin users whereas it was 8.6% in oral antidiabetic using patients in Colloredo-Mels et al's study (19). According to this study the chronic liver disease incidence was not higher in diabetics than in the normal population. They concluded that insulin treatment was not a risk factor for HBV infection. And in another study carried out among 210 insulin user diabetic patients by Olio et al (20), the positivity of HBsAg was 9 % in diabetics where as it was 2.9 % in nondiabetics. Our study results also support the recently documented studies that there is no relation between the type of antidiabetics used and HBV infection. According to Olio et al (20), the newer diabetics have lesser HBV positivity than older diabetic patients. According to our study results there is not any association between the period of antidiabetic use and HBV, HCV infection incidence. Colloredo-Mels et al (19) concluded that increased age and HCV infection frequency was higher than HBV infection and they also concluded that age was an independent factor. According to our study results there is no relation between age and HBV infection. As a result HBV incidence is similar with the normal population where as HCV infection is higher among diabetics than in the normal population. However, to clarify the incidence of HCV infection among diabetic patient, we need further studies.

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