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Original Research Article

The Relationship between Hepatitis C Virus Infection and Diabetes Mellitus Type 2

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ABSTRACT

To determine the relationship between hepatitis C virus infection and Diabetic mellitus type 2 , twenty patient's with diabetic mellitus type 2 aged (30-61) years old have been investigated from 01/11/2014 to 01/02/2015 and compared with fifteen parentally healthy individuals. All the studies groups were carried out to measure anti-HCV Abs by enzyme linked immunosorbent assay (ELISA), There was significant elevation (P≤0.05) in the HCV Abs compared with control groups .The percentage of HCV Abs was 15% and there was highly significant (P≤0.01) differences between studied group, while there was non-significant differences (P≥0.05) between patients groups according to age and gender compared with control groups. These results indicated that there is an association between HCV infection and diabetes mellitus.

Keyword: Hepatitis c virus; diabetes mellitus type 2; antibodies

INTRODUCTION

Hepatitis C virus (HCV), RNA single strand positive sense genome virus, was first recognized as a separate disease entity in 1975 when the majority of transfusion-related hepatitis were found not to be caused by the only two hepatitis viruses recognized at that time that is Hepatitis A virus and Hepatitis B virus. The disease at that time was called "non-A non-B hepatitis''. The discovery of hepatitis C genome in 1989 has now led to the realization that this virus is a major health problem worldwide.

HCV is most efficiently transmitted through transfusion of infected blood, transplantation of infected organs, and sharing injection drug equipments. The majority of persons with newly HCV infection are asymptomatic. Only 20% of them develop symptoms such as fatigue, abdominal pain, poor appetite, or

jaundice, usually within 4–12 weeks [1].Hepatitis C virus (HCV) infection is an important public health problem which currently affects more than 170million people (about 3% of world population) out of which 55-80% have chronic infection [2].Hepatitis C virus (HCV) has been identified as one of the leading causes of chronic liver disease with serious sequel as the end stage of cirrhosis , liver cancer , liver fibrosis ,cirrhosis , hepatocellular carcinoma (HCC), and is the primary cause for liver transplantation in the western world [3,4] .Moreover, chronic HCV infection has been associated with several extra hepatic complications. The suggestion that HCV may be associated with type 2 diabetes mellitus (type 2 DM) was first made by Allison in 1994. Since then, scores of observational studies assessing the association between HCV and type 2 DM have been published [5].

The epidemiological link between T2DM and HCV has been investigated from two perspectives. Various studies have shown high HCV seropositivity among patients with T2DM as compared to the control group, prevalence being two to seven times higher in the diabetic group.

The pathogenesis of diabetes in patients with HCV infection remains unclear though it has been implicated that insulin resistance plays an important role and is related to fibrosis score [6]. Insulin resistance in muscular, hepatic and adipose tissues as well as hyperinsulinemia, seem to be pathophysiologic bases for hepatogenous diabetes. An impaired response of the β-islet cells of the pancreas and the hepatic insulin resistance are also contributing factors. Diabetes develops when defective oxidative and non-oxidative muscle glucose metabolism develops. Non-alcoholicfatty liver disease (NAFLD), alcoholic cirrhosis, chronic hepatitis C, and hemochromatosis are more frequently associated with hepatogenous diabetes [7].Series of studies found that prevalence of HCV infection is higher in patients with diabetes than in those without diabetes9-12. Elevations of aminotransferases greater than eight times the upper limit of normal which reflect either acute viral hepatitis or liver injury and chronic mild elevations of transaminases are frequently found in type 2 diabetic patients [13]. Liver enzymes conventionally associated with liver dysfunction (aspartate aminotransferases (AST) and alanine aminotransferases (ALT)) may predict diabetes [8].It might be then thought that HCV could trigger an immune reaction against the cell that leads to diabetes. In this case, a possible pathogenic mechanism could be molecular mimicry, because HCV share sregional amino acid homology with GADautoantibody (GADA), one of the mainislet cell antigens (63).HCV could contribute to latent autoimmune diabetes in adults, a slowly evolving autoimmune insulinitis that represents between4 and 34% of all diagnosed diabetes in adults [9]. The aim of the present study was to determine the relationship between hepatitis C virus infection and type 2 diabetes mellitus

MATERIALS AND METHODS

The study was carried out on twenty patients suffering from Diabetic mellitus type 2 that introduced to Baghdad hospital, AL- Yarmok hospital during the period from first of November 2014 until January 2015.The ages of the total patients were ranged from (30-61)years. Fifteen samples of healthy individuals 7 female and 8 male were studied as control groups of same ages and sex. Blood samples (5 ml) were collection by disposable syringe into gel tubes and stand at room temperature until the coagulant was form. Then, the samples were centrifuged at 3000 rpm. for 5 min All samples were marked by the name, day and numbering and stored at (-20Ċ) until carried out to detect anti HCV by ELISA test according to leaflet of kit[10].

STATISTICAL ANALYSIS

Comparison of paired data from the group of subject was done using t-test (t), while correlation between groups were analysed using person chi-square and least significant difference(LSD) test was used to significant compression between means in this study. The computer program which used was SPSSV.11-5[11].

RESULTS AND DISCUSSION

The results of the present study showed that there was a significant elevation (P<0.05) in the ratio absorbance of HCV Abs (0.77±0.09) compared to control group (0.27±0.05) as shown in fig1 and fig 2.

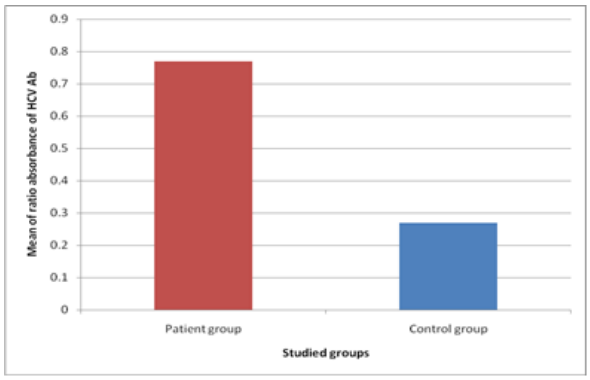

Fig. 1: Mean ratio absorbance of HCV Abs in patients with DM type 2 and control group

The prevalence of HCV Abs was 15 %(3/20) and there was highly significant (P<0.01) differences between study groups as shown in fig. 2.

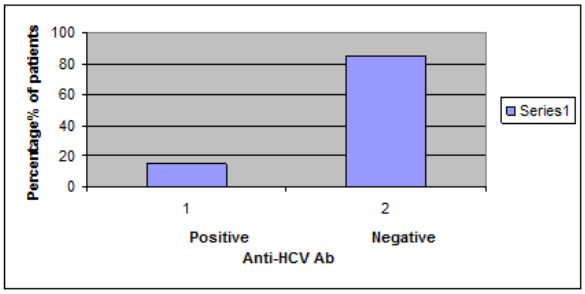

Fig. 2: Percentage distribution of anti-HCV Abs in sera of patients with DM type 2

Also, the statistical analysis revealed that there was non-significant differences (P>0.05) when compared between studied groups according to age and gender as shown in table 1 and 2.

In this study we have tried to analyze the association between hepatitis C virus infection and diabetic mellitus type 2.The results of the present study were agreement with many other several studies. One study found that the seroprevalence rate of anti-HCV in type II diabetic Patients and non-diabetic controls was 9.9% and 3.3%, respectively [1].In another study, we found high prevalence of HCV infection in patients with T2DM as compared to the Control group comprising of healthy volunteer blood donors (13.7% vs. 4.9%)[2].

The findings also agree with another study conducted earlier in the country albeit with a small sample use and no control group who recorded prevalence of 36% among diabetics[12],while HCV infection prevalence in the diabetes, type 2 DM, and control groups was 1.3%, 1.4% and 0.6%, respectively in study done by [13].

In a study done by Sadik [3] the prevalence rate was 31.5%, while, another local study by Khakar [14] showed the prevalence of HCV infection in diabetics to be 17.27% with increased vulnerability. It is not possible to forward easily for the cause of this increased prevalence of HCV in diabetic patients. But there are two possibilities; the first possibility might be in association of diabetic patients for HCV as a result of repeated exposure for finger prick injury, daily insulin injection and immune compromised state a result of diabetes. The other possibility might be due to the direct and/or indirect effect of HCV infection on glucose metabolism [1].

As per experimental researches, it seems that the virus itself through its core protein can modify the metabolic profile of HCV infected patients which leads to development of type II diabetes mellitus. Mechanistic studies have revealed that HCV encoded proteins may cause post receptor defects in insulin receptor substrate 1 (IRS-1). It may also associate with

Table 1: Mean level of anti-HCV Abs among studies group and distribution of anti-HCV Ab according to age

Studied groups	HCV Ab mean ± SE	Age mean ± SE	LSD for HCV Ab	LSD for Age	HCV Ab Probability	Age Probability
Patients group	0.77 ± 0.09	45.2 ±2.2	0.49	3.13	Significant (P<0.05)	Non-significant (P>0.05)
Control group	0.27 ± 0.05	42.1 ± 2.4				

Table 2: The percentage distribution of anti-HCV Abs according to gender

Studied groups	Male	Female	Pearson Chi-square	DF	Sig.
Patients group	7	13	0.486	1	0.5
Control group	7	8			

the insulin receptor (IR) and insulin signaling defects in hepatic IRS-1 tyrosine phosphorylation and phosphatidylinositol 3-kinase (PI3k) activation that may contribute to development of insulin resistance and subsequent development of type 2 diabetes mellitus [15,16].

The hypothesis that HCV core protein can modify the metabolic profile of HCV infected patients which lead to development of type II diabetes mellitus is also supported by Experimental data derived from transgenic mice infected with hepatitis C core protein that recently demonstrated that this protein induces insulin resistance directly, and tends to occur early in the course of infection, prior to development of steatosis or fibrosis [17]. Among humans with chronic hepatitis C (CHC) infection, it has been shown that insulin signaling in the liver is altered by defects in IRS-1 tyrosine phosphorylation and phosphatidyl inositol 3kinase activation, thus possibly contributing to insulin resistance [18].

It is also suggested that the proinflammatory cytokine, TNF-α, may mediate this process. TNF-α is upregulated in patients with chronic hepatitis C (CHC) and this cytokine has been shown to interrupt insulin signaling via reducedtyrosine phosphorylation of IRS-1 and decreased ability of IRS-1 to associate with the

insulin receptor. Data to support a role for TNF-α in the genesis of insulin resistance found in insulin resistant transgenic mice infected with hepatic C core protein. When treated with anti-TNF-α, insulin sensitivity significantly improves [19, 20]. More recent evidence suggests that the hepatitis C virus may further alter insulin signaling by upregulating expression of the protein suppressor of cytokine signaling 3, resulting in decreased activation of downstream components of insulin receptor signaling (IRS), and altered expression of sterol regulatory binding protein 1c, which is important in de novo lipogenesis [21,22].

CONCLUSION

These results indicated that there is an association between HCV infection and diabetes mellitus. We further recommend detection of HCV RNA for a study designed with prospective cohort to be conducted for better extrapolation of HCV being a risk factor for diabetic type II.

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