Association of HCV infection and diabetes mellitus type 2 in Damietta

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Abstract: Background: Hepatitis C virus (HCV) infection and diabetes mellitus are the major public health challenges with increasing morbidity and mortality disease burden. Several studies reported that HCV infection may also contribute to the development of diabetes mellitus. **Objective:** to clarify the presence of any possible relationship between HCV and type 2 Diabetes mellitus and the prevalence of diabetes mellitus in HCV seropositive patients in Damietta. **Subjects and Methods:** This is a case control study done on 70 HCV positive patients as a case group who were attended to Damietta University Hospital and 30 healthy individuals as a control group, during the period from May 2016 to April 2017. An informed consent was taken from all subjects participating in this study. All subjects included in this study were subjected to: Full history taking, Clinical examination and Laboratory investigation in the form of (complete blood picture, liver enzymes, S.albumin, T.bilirubin, fasting & 2hpp blood glucose, fasting plasma insulin and screening for HCV and HBV). **Results**: The results of present study showed no statistical significant differences between case and control groups as regard to age, sex and total leukocytic count. while there were statistical significant differences between case and control groups as regard to fasting plasma insulin, fasting plasma glucose,2hpp plasma glucose, ALT, AST, albumin, bilirubin, cholesterol and triglycerides. **Conclusions**: Many epidemiological studies have shown an association between T2DM and CHC. The processes through which HCV is associated with DM seem to involve direct viral effects, IR, proinflammatory cytokines, chemokines, suppressors of cytokine signalling, and other immune-mediated mechanisms.
[Mohammed I. Aref, Mekky A. Ali, Mahmoud F. Salem and Mohammed E. Ahmed. **Association of HCV infection and diabetes mellitus type 2 in Damietta.** *Nat Sci* 2017;15(7):124-127]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). http://www.sciencepub.net/nature. 17. doi:10.7537/marsnsj150717.17.

Keywords: Hepatitis C infection, Type 2 Diabetes mellitus, Insulin resistance

1. Introduction

Hepatitis C virus (HCV) infection and diabetes mellitus are the major public health challenges with increasing morbidity and mortality disease burden (**Zimmetet al., 2014)**. 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 and liver cancer (**Elfiky et al., 2013**). Diabetes mellitus is a complex disease with pathophysiology that includes increased hepatic glucose production, defects in insulin secretion, and/or insulin resistance (**Cavaghan et al., 2000**). Diabetes mellitus is a chronic disease of metabolism causing abnormal glucose homeostasis (**Imam et al., 2012**). Diabetes has been also recognized as part of the spectrum of HCV-associated diseases (**Allison et al., 1994**). Several studies reported that HCV infection may alsocontribute to the development of diabetes, and higher prevalenceof type 2 diabetes mellitus has been observed in thedeveloped world (2% to 9.4%) in patients with HCV infectionthan in those with other forms of chronic hepatitis (**Naing et al., 2012**). There are several organized factors which influence the development of diabetes among HCV-infected patients like age, sex, family history of diabetes and African-American race (**El hawary et al., 2011**). HCV is a multifaceted infection affecting different processes such as mitochondrial function, insulin resistance, lipid metabolism, and signaling pathways among others (**Eslam et al., 2014**). Insulin resistance (IR) and diabetes can develop at any stage of HCV infection. Multiple mechanisms have been accounted for insulin resistance and development of diabetes in patients with chronic hepatitis C. It promotes IR mainly through interfering with insulin signaling pathway in hepatocytes, increasing inflammatory response with production of cytokines such as TNF alpha and IL-6 and increasing oxidative stress (**Huang et al., 2007**).

2. Subjects and Methods

One hundred individual were included in the present study. They were selected from Al-Azhar University Hospital (New Damietta); during the period from April 2016 to Mrach 2017.

They were divided into two groups:

Group (1): (Case group): included 70 individuals with seropositive hepatitis C virus. They were 43 males and 27 females with their ages ranged from 24 to 61 years with a mean age± SD is 45.34 ± 9.74 years.

Group (2) (Control group): Included 30 healthy individuals. They were 21 males and 9 females with their ages ranged from 28 to 60 years with a mean age ± SD of 44.07 ± 9.14 years.

Inclusion criteria

HCV seropositive patients, with or without presence of liver cirrhosis between the age of 18 and 75 years, both males and females visiting the outpatient or admitted in Gastroenterology and Hepatology department in Al-azhar University Hospital (New Damietta).

Exclusion criteria:

Patients with liver cancer, having end stage renal disease or coexisting viral infection like hepatitis B surface antigen positive patients, and pregnant females were excluded from the study.

Methods:

All included individuals were submitted to:

1- Full history taking (e.g., name, age, sex, residence, present and past history, family history).

2- Detailed clinical examination, that divided into two phases; the first is the clinical examination and the local is abdominal examination. Both were done in systematic manner (inspection, palpations, percussion and auscultation).

3- Laboratory investigations:

- Complete blood picture (CBC),
- Liver enzymes (ALT, AST), serum total bilirubin, serum albumin, serum cholesterol and serum triglycerides.
- Evaluation of fasting and 2 hour post prandial plasma glucose.
- Evaluation of fasting plasma insulin.

Statistical presentation and analysis of the present study was conducted using the mean, standard deviation, student t- test, linear correlation coefficient tests by SPSS V17 (statistical program for social science). Description of quantitative variables by mean, SD, rang and description of qualitative variables by number and percentage. A value of $P \leq 0.05$ was.

3. Results

Table (1): Comparison between case and control groups as regard to age, sex, liver enzymes, albumin t.bilirubin, cholesterol

Parameters		Groups		P-value	Sig.
		Case group	Control group		
Age (Years)	**Mean ±SD**	**45.34 ± 9.74**	**44.07 ± 9.14**	**0.54**	**N.S.**
Fasting plasma insulin	**Mean ±SD**	**14.55 ± 11.96**	**8.27 ± 4.93**	**0.007**	**S.**
Fasting plasma glucose (mg/dl)	**Mean ±SD**	**109.8 ± 53.47**	**88.73 ± 20.0**	**0.038**	**S.**
2hpp plasma glucose (mg/dl)	**Mean ±SD**	**187.9 ± 101.7**	**148.2 ± 35.6**	**0.040**	**S.**
ALT (IU/L)	**Mean ±SD**	**89.7 ± 57.8**	**29.3 ± 13.6**	**<0.001**	**V.H.S**
AST (IU/L)	**Mean ±SD**	**107.0 ± 78.4**	**31.87 ± 15.9**	**<0.001**	**V.H.S**
S.Albumin (gm/dl)	**Mean ±SD**	**3.83 ± 0.54**	**4.25 ± 0.3**	**<0.001**	**V.H.S**
T.Bilirubin (mg/dl)	**Mean ±SD**	**1.2 ± 0.89**	**0.57 ± 0.25**	**<0.001**	**V.H.S**
S.Creatinine (mg/dl)	**Mean ±SD**	**0.88 ± 0.16**	**0.87 ± 0.19**	**0.801**	N.S
Cholesterol (mg/dl)	**Mean ±SD**	**170.26 ± 48.3**	**210.43 ± 48.6**	**<0.001**	**V.H.S**
Triglycerides (mg/dl)	**Mean ±SD**	**156.6 ± 30.9**	**109.0 ± 24.0**	**<0.001**	**V.H.S**
Haemoglubin (gm/dl)	**Mean ±SD**	**11.49 ± 1.3**	**12.73 ± 1.1**	**<0.001**	**V.H.S**
WBCs	**Mean ±SD**	**6.01 ± 2.61**	**6.7 ± 2.28**	**0.209**	N.S
Platelet	**Mean ±SD**	**173 ± 80**	**280 ± 56**	**<0.001**	**V.H.S**

*P-value<0.05 is significant

The results of present study showed no statistical significant differences between case and control groups as regard to age, sex and total leukocytic count. while there werestatistical significant differences between case and control groups as regard to fasting plasma insulin, fasting plasma glucose,2hpp plasma glucose, ALT, AST, albumin, bilirubin, cholesterol and triglycerides.

Table (2): Correlation between fasting plasma insulin and other parameters.

	Fasting plasma insulin	
	r	**P-value**
Age (Years)	0.414	<0.001
Fasting plasma glucose (mg/dl)	0.824	<0.001
2hpp plasma glucose (mg/dl)	0.798	<0.001
Albumin	- 0.380-	0.001
T.Bilirubin	0.261	0.029

**. Correlation is significant at the 0.01 level (2-tailed). *. Correlation is significant at the 0.05 level (2-tailed)

In the present study, there was positive correlation between fasting plasma insulin and age, fasting plasma glucose, 2hpp plasma glucose and T.bilirubin, while there was negative correlation between fasting plasma insulin and S.albumin.

4. Discussion

Hepatitis C virus (HCV) infection and diabetes mellitus are the major public health challenges with increasing morbidity and mortality disease burden (**Zimmet et al., 2014**).

HCV is a multifaceted infection affecting different processes such as mitochondrial function, insulin resistance, lipid metabolism, and signaling pathways among others (**Younossi et al., 2014**).

Diabetes has been also recognized as part of the spectrum of HCV-associated diseases. Diabetes mellitus is a complex disease with pathophysiology that includes increased hepatic glucose production, defects in insulin secretion, and/or insulin resistance (**Cavaghan et al.,2000**).

An estimated 200 million people are infected worldwide with chronic hepatitis C (CHC) and insulin resistance (IR) is one of the biochemical features of hepatitis C virus (HCV) infection. Insulin resistant is defined as cells becoming resistant to the action of insulin. It provides a protective mechanism to maintain a normal insulin level. Previous studies had shown that IR is an early regulatory event in chronic HCV infection that accelerates liver fibrosis **(Moucari et al., 2008)**.

Studies have shown that along with multiple host factors, the virus itself can perpetuate IR, hepatic steatosis and diabetes, which reduces the likelihood of sustained virological response (SVR) and increases the risk of CHC complications and progression to cirrhosis **(Harrison et al., 2012).**

The present study was designed to investigate the association between HCV seropositive patients and prevalence of type 2 diabetes mellitus. The subjects were classified into 2 groups:

(1) **Case group** which included 70 patients with seropositive HCV infection.

(2) **control group** which included 30 healthy individuals.

In the present study, there was no statistically significant difference between case and control groups as regard age and sex distribution, with males predominate in both groups.

In the present work, there were statistically significant differences between case group and control group as regard laboratory parameters including Hemoglobin, Platelets, lipid profiles, blood glucose levels and liver function tests. These results are in agreement with those reported by **Kim et al. (2009)** who reported that, there was no significant difference between case group and control group as regard liver function, lipid profile and fasting plasma glucose.

In the present work, there was highly statistically significant increase in the incidence of IR among case group in comparison to control group. In addition, there was highly statistically significant increase of fasting insulin in case group when compared to corresponding values in control group. The highest increase of fasting insulin was in case group **(Delgado-Borrego et al., 2010).**

Hepatitis C virus is able to decrease insulin sensitivity and IR has been systematically associated with advanced fibrosis and fibrosis progression **(Petta et al., 2008).** Both IR and hepatic steatosis have been closely associated with progression of hepatic fibrosis in patients with HCV infection ***(Lonardo et al., 2004).***

In the present work there was statistically significant progression of liver fibrosis with increase of IR Recently, several reports have suggested that IR may contribute to the progression of fibrosis ***(Fartoux et al., 2005).*** IR may directly stimulate the proliferation of hepatic stellate cells (HSCs) promoting collagen I synthesis or IR-induced hepatic lipid accumulation and generation of Reactive oxygen species (ROS) can activate HSCs, initiating progression of fibrosis to cirrhosis ***(Paradis et al., 2001).***

The results of this study are in agreement with that reported in the recent publication on Insulin resistance and chronic hepatitis C in non-diabetic patients done by **Souza and cols (2011)** who concluded that "Insulin resistance is often present in patients with chronic hepatitis C, and this parameter is associated with more advanced HCV-related hepatic fibrosis"**.**

In the present work, there was significant positive correlation between serum fasting plasma insulin and age, blood glucose levels and T.bilirubin. These results are in agreement with **Petta et al. (2008)** who reported that, insulin resistance and diabetes increase fibrosis in the liver of patients with genotype-1 HCV Infection. They concluded that, in subjects with CHC resulting from G1-HCV, IR and overt diabetes are major determinants of advanced fibrosis, regardless of the degree of steatosis, mainly in the presence of severe necro-inflammation.

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7/3/2017