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HEPATITIS C VIRUS IGG AND CYTOMEGALOVIRUS IGG PREVALENCE IN PATIENTS WITH DIABETES MELLITUS

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Abstract

Background: Hyperglycemia and abnormal glucose metabolism were produced by known pathologic mechanisms; the etiology of type 2 diabetes mellitus (T2DM) is still enigmatic. Complex interaction of genetic, metabolic, and environmental factors contributes to T2DM development. The study aimed to detect of prevalence of HCV and cytomegalovirus in type 2 diabetes mellitus. **Patients and methods:** A case-control study done on 95 patients confirmed with T2DM. In addition, 95 apparently healthy individuals were designated as a control group. The present study was initiated to evaluate sero-prevalence of two viral antibodies including (CMV IgG, HCV IgG) beside Hepatitis B surface antigen (HBsAg) in diabetic patients in comparison to the control group. **Results:** There was a highly statistically significant difference between groups according to blood pressure and systolic blood pressure and mean blood pressure (mmHg). There was statistically significant increase in HCVAb (IgG) positive patients in diabetic group compared to control group. There was statistically significant increase in Cytomegalovirus IgG positive patients in diabetic group compared to control group. There was no statistically significant association between HCVAb (IgG) and Cytomegalovirus IgG in diabetes group (n=95). **Conclusion:** There is possible strong association between HCV, and cytomegalovirus in type 2 diabetes mellitus patients. The rate of seropositive anti-HCV is 2 times higher in type 2 DM patients than non-diabetic control subjects.

Keywords: HCVAb (IgG) ; Cytomegalovirus IgG ; SBP ; T2DM

INTRODUCTION

Diabetes Mellitus is a metabolic disorder of multiple causes characterized by chronic hyperglycemia and disorders of carbohydrate, fat, and protein metabolism. It results from defects in insulin action (type 2), or a combination of these factors **(1)**.

Rapid incidence and fast growing of DM around the world, makes it as a major public health concern. According to the International Diabetes Federation (IDF), by 2045 the expected cases will be 629 million of people having diabetes **(2)**.

Cytomegalovirus (CMV) is one of the most common herpes viruses worldwide, which can cause an asymptomatic lifelong infection with multiple severe complications **(3)**. Presence of CMV IgM alone indicates recent infection IgG without IgM indicates remote infection. A titre increase in sequential samples of IgM may indicate ongoing active infection **(4)**. Human CMV is one of the viral

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factors that are supposed to be linked with the incidence of DM, as a result of its capability to induce β-cells damage **(5)**.

The main site of glucose metabolism and its hormonal changes is the liver, which has a very common relationship with diabetes. Several studies have described the association of diabetes mellitus and solid cancer, particularly with HCC, which most of patients with liver cirrhosis from HBV and HCV have (60%) of glucose intolerance and DM type 2 **(6)**.

Therefore, Hepatitis C virus (HCV) is another significant health problem, which affects over than 180 million of people worldwide, and is considered as a major cause of high morbidity and deaths, that is because its further complication may lead finally to liver cirrhosis and HCC **(7)**. The aim of the present study was to assess the prevalence of HCV and cytomegalovirus in type 2 diabetes mellitus.

PATIENTS AND METHODS:

This case control study included 190 patients with type 2 diabetes mellitus. The study was performed at Internal Medicine Department and Microbiology Department, Zagazig University Hospitals from July to October 2020. The study was approved by the Zagazig University Institution Review Board (IRB), official permission from study setting department and an informed written consent was obtained from all patients before they joined the study.

Inclusion and Exclusion criteria:

Adult patients with type 2 DM of both sexes. While, patients with Type 1 diabetes mellitus ,Patients with end-organ failure (hepatic/renal or cardiac),patients with MODY onset diabetes mellitus , patients with evidence of malignancy and patient refusal.

All patients were subjected to full history, clinical examination and routine laboratory investigations.

Specific investigations:

1- HCV Ab(IgG)using a commercial electrochemiluminescence assay (ECLIA): Immunoassay for the in vitro qualitative detection of antibodies to HCV in human adult serum.
2- CMV IgG using a commercial electrochemiluminescence assay (ECLIA): For the quantitative determination of IgG Antibodies to Cytomegalovirus (CMV) in serum.

Results were determined via a calibration curve which is instrument specifically generated by 2-point calibration and a master curve provided via the reagent barcode

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.The following tests were done: Independent-samples t-test of significance was used when comparing between two means.Chi-square (x2) test of significance was used in order to compare proportions between qualitative parameters.The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: P-value <0.05 was considered significant and P-value <0.001 was considered as highly significant.

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RESULTS:

The results of the present study showed no statistically significant difference between groups according to demographic data **(Table 1)**.There was a highly statistically significant difference between groups according to blood pressure **(Table 2)** and systolic blood pressure and mean blood pressure (mmHg) **(Table 3)**. There was statistically significant increase in HCVAb (IgG) positive patients in diabetic group compared to control group **(Figure 1)**. There was statistically significant increase in Cytomegalovirus IgG positive patients in diabetic group compared to control group **(Table 4)**. There was no statistically significant association between HCVAb (IgG) and Cytomegalovirus IgG in diabetes group (n=95) **(Table 5**). There was highly statistically significant Association between Cytomegalovirus IgG and HCVAb(IgG) with diabetes group, while HBsAg significant with diabetes group **(Table 6**).

Table (1): Comparison between diabetes group and control group according to demographic data.

Demographic data	**Diabetes Group** ***(n=95)***	**Control Group** ***(n=95)***	**Total (n=190)**	**Test**	**p-value**
Sex					
Male	41 (43.2%)	48 (50.5%)	89 (46.8%)	x^2= 1.036	0.309
Female	54 (56.8%)	47 (49.5%)	101 (53.2%)		
Age (years)					
Mean±SD	55.17±9.22	53.45±11.77	54.31±10.58	t=1.118	0.265
Range	36-77	37-83	36-83		
BMI [wt/(ht)^2]					
Mean±SD	31.19±3.56	30.17±3.74	30.68±3.68	t=1.918	0.057
Range	22.49-40.4	21.48-41.15	21.48-41.15		

t-Independent Sample t-test; x^2: Chi-square test; p-value>0.05 NS

Table (2): Comparison between diabetes group and control group according to blood pressure.

HTN	**Diabetes Group** ***(n=95)***	**Control Group** ***(n=95)***	**Total (n=190)**	***x^2***	**p-value**
Normotensive	37 (38.9%)	64 (67.4%)	101 (53.2%)	15.490	<0.001**
Hypertensive	58 (61.1%)	31 (32.6%)	89 (46.8%)		

*x^2: Chi-square test; **p-value <0.001 HS*

Table (3): Comparison between diabetes group and control group according to blood pressure (mmHg).

Blood pressure (mmHg)	**Diabetes Group** ***(n=95)***	**Control Group** ***(n=95)***	**Total (n=190)**	**t-test**	**p-value**
Systolic (mmHg)					
Mean±SD	143.95±20.91	125.32±15.55	124.63±18.39	6.968	<0.001**
Range	120-180	90-170	90-180		
Diastolic (mmHg)					

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Mean±SD	78.37±12.66	80.16±9.30	79.26±11.11	-1.11	0.268
Range	50-110	60-100	50-110		
Mean BP (mmHg)					
Mean±SD	103.55±14.61	95.16±10.95	94.35±12.90	4.479	<0.001**
Range	75-130	70-123	65-130		

t-Independent Sample t-test;p-value>0.05 NS

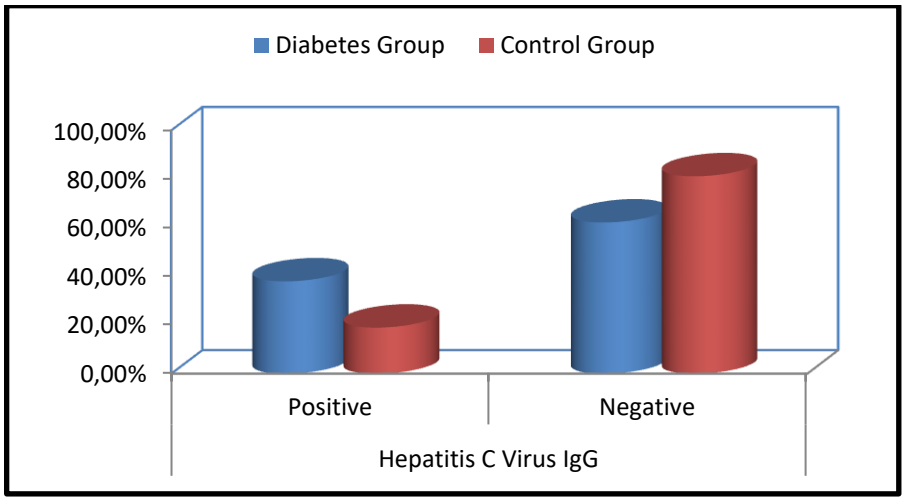

Fig.(1): Bar chart between diabetes group and control group according to HCVAb(IgG).

Table (4): Comparison between diabetes group and control group according to Cytomegalovirus IgG.

Cytomegalovirus IgG	**Diabetes Group *(n=95)***	**Control Group *(n=95)***	**Total (n=190)**	**x2**	**p-value**
Positive	65 (68.4%)	47 (49.5%)	112 (58.9%)	7.047	0.008*
Negative	30 (31.6%)	48 (50.5%)	78 (41.1%)		

*x^2: Chi-square test; *p-value <0.05S*

Table (5): Association between HCVAb(IgG) and Cytomegalovirus IgG in diabetes group (n=95).

Cytomegalovirus IgG		HCVAb(IgG)		**Total**	**Chi-square test**	
		PositiveHCVAb(IgG)	**Negative** HCVAb(IgG)		**x2**	**p-value**
Positive CMV	No.	27	38	65	1.161	0.281
	%	28.4%	40.0%	68.4%		
Negative CMV	No.	9	21	30		
	%	9.5%	22.1%	31.6%		
Total	No.	36	59	95		
	%	37.9%	62.1%	100.0%		

x^2: Chi-square test; p-value>0.05 NS

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Table (6): Association between HBsAg, HCVAb(IgG) and Cytomegalovirus IgG with diabetes group (n=95).

	Diabetes Group *(n=95)*	**x2**	**p-value**
Cytomegalovirus IgG	65 (68.4%)	95.738	<0.001**
Hepatitis C Virus IgG	36 (37.9%)	41.990	<0.001**
Hepatitis B Virus Ag	10 (10.5%)	8.5243	0.004*

*x^2: Chi-square test; *p-value<0.05 S; **p-value <0.001 HS*

DISCUSSION:

Human CMV is one of the viral factors that are supposed to be linked with the incidence of DM, specially Type 1as a result of its capability to induce β- cells damage **(5)**. Clinical reports suggest that HCMV may be increase the risk of graft failure and cirrhosis in HCV seropositive liver transplant recipients. In addition, the contribution of HCV-RNA to CMV infection HCV seropositive renal transplant recipients, whether the co-infections with CMV and HCV potentiate the risk of DM is still unclear **(8)**.

Hepatitis B virus (HBV) is small double DNA strands that belongs toOrthohepadnavirus genus of the Hepadnaviridae family, which resulting in both acute and chronic infections **(9)**. More than 80% of Hepatocellular carcinoma (HCC) cases has been implicated to HBV infection. Chronic HBV infection persisting in liver tissue is connected mostly with elevated liver inflammation, oxidative damage, chronic hepatocytes and eventually tumor development **(10)**. Besides hepatic disorder, HBV chronic infection is associated with wide spectrum of extrahepatic manifestations **(10)**.

The main site of glucose metabolism and its hormonal changes is the liver, which has a very common relationship with diabetes. Several studies have described the association of diabetes mellitus and solid cancer, particularly with HCC, which most of patients with liver cirrhosis from HBV and HCV have (60%) of glucose intolerance and DM type 2 **(6)**. Patients with Type-2 DM have higher risk to be infected with hepatic viruses, as hepatitis B or C virus **(11)**.

In this study we aimed to detect and evaluate the potential association between HCVAb (IgG) and cytomegalovirus IgG in type 2 diabetes mellitus patients.This study was conducted as a case-control study done on 95 patients confirmed with type 2 diabetes mellites. In addition, 95 apparently healthy individuals were designated as a control group.

In our study the demographic data findings show that the two groups (diabetic and control) matched with each other, as we found that there is no significant difference according to gender and age as (p value=0.309 ,0.265) respectively. These results are agree with Nayak et al.,(12) who reported that type 2 diabetes mellitus affected by various risk factor in terms of demographic data (age and sex).

Concerning blood pressure, our study showed that there is highly statistically significant difference between the two groups (p value <0.001) as shown in table (2) and figure (1). About 61.1% of diabetic group suffering from hypertension in comparison to 32.6% in control group. These results

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describe the potential relationship between type 2 DM and hypertension in which they elicit each other. Type 2 DM can also be a risk factor for developing and triggering hypertension as it is said by **(13)**.

The attainable results in our study was compared to a study of **Ambachew et al.,(11)** revealed that hepatitis C virus infection is an important risk factor for the development of diabetes mellitus. Also, **Jadoon et al., (14)** mentioned that there was a strong association between HCV and T2DM and significantly higher prevalence of HCV infection in diabetics as compared to the control group.

Our study is supported by the results of **Hum and Justine et al., (15)** stated HCV infection is associated with a higher prevalence of type 2 diabetes mellitus (T2DM). **Chen et al., (16)** found the rate of seropositive anti-HCV is 2.8 times higher in type 2 DM patients than non-diabetic control subjects.

Also **Shoeb et al., (17)** agreed with our finding that, they found that CMV – HCV coinfection is predominant in Egypt, and CMV co-infection may influence the HCV treatment outcome, despite it failed to have statistical significance.

CONCLUSION:

There is possible strong association between HCV, and cytomegalovirus in type 2 diabetes mellitus patients. The rate of seropositive anti-HCV is 2 times higher in type 2 DM patients than non-diabetic control subjects.

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