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Sero-prevalence of Hepatitis C Virus Antibody among Type 2 Diabetic Patients Attending the Outpatient Clinic of Internal Medicine Department at Zagazig University Hospitals: Across-sectional descriptive study

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ABSTRACT

Background: Diabetes Mellitus (DM) and viral hepatitis C virus (HCV) are two major health problems of economic and social burden in Egypt. HCV is highly prevalent in type2 diabetic patients (T2DM patients) as it interferes with the insulin-signaling pathway. Also T2DM is one of extra-hepatic manifestations of HCV. Major known modes of transmission for HCV include injectable drug use, dental procedures, barberin g, tattooing, body piercing and sharing contaminated materials. ***Aim and objective:*** To evaluate the sero-prevalence of HCV antibodies among T2DM patients at the outpatient clinic of Internal Medicine Department at Zagazig University Hospitals aiming to determine the magnitude of HCVab among these patients. ***Patients and methods:*** This study is a cross-sectional descriptive study conducted on T2DM patients. Each patient filled three questionnaires: the first about socio-demographic data, the second includes patient history of T2DM and assessment of knowledge about the disease and the third one for assessment of knowledge, prevalence and risk factors of HCV. Blood samples were obtained from all patients for testing HCVab. ***Results:*** The prevalence of HCVab among T2DM participants is 31.3%. The prevalence is statistically higher in type2 diabetic males with the age range between 27 – 85 years old, diagnosed as T2DM for more than 10 years, had a family history of HCV and had risk factors for HCV transmission. ***Conclusion:*** The high prevalence of HCVab in T2DM patients (31.3%) may be because the majority of participants were of low socioeconomic level, had positive family history for HCV and were subjected to risk factors for HCV transmission.

Keywords: Diabetes mellitus, Hepatitis C, type2 diabetic patients.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a major global health problem that is rapidly developing due to increasing frequency of obesity and sedentary lifestyle [1]. The chief cause of morbidity and mortality in T2DM patients is cardiovascular disease. It is also a primary cause for non-traumatic lower limb amputation, severe optic complications, and end-stage renal disease [ESRD] [2].

Hepatitis C (HCV) is a global infectious disease. According to the World Health Organization (WHO), 130-170million people are chronically infected with HCV and 3-4million new cases are diagnosed annually worldwide [3].The main route of transmission for HCV is the parenteral route including blood transfusion, intravenous injections [4].

The relationship between DM and the liver has been known since 30 years ago. Many studies reporting that HCV were detected more frequently in patients with DM because of their association with diseases that suppress the immune system [5].

HCV interferes with the insulin-signaling pathway by modifying cellular gene expression by up-regulation of inflammatory cytokine tumor necrosis factorα, hypo-phosphorylation of insulin receptor substrate1 and 2, phosphorylation of protein kinase B, up-regulation of gluconeogenic genes and accumulation of lipids and targeting of lipid storage organelles [6].

So we aim in this study to detect the magnitude of HCVab among type2 diabetic patients.

PATIENTS AND METHODS

This is a Cross sectional study was conducted in out-patient clinic of Internal Medicine Department at Zagazig University Hospitals, Sharkia Governorate, Egypt from March (2018) to October (2018). The study included a total number of 227 type 2 diabetic patients.

Inclusion criteria:

Type 2 diabetic patients; regardless of gender, body weight, educational level or socioeconomic levels attending the out-patient clinic of Internal Medicine Department at Zagazig University hospitals were included in the study

Exclusion criteria:

- Type 1 diabetic patient.
- Age more than 85 and less than 20 years old.

Sample size:

As the total number of type2 diabetic patients attending the outpatient clinic at Zagazig University Hospital is 600 in 6 months and the prevalence of HCVab among these patients was 38.7% according to [7]; with CI 95%, the sample was calculated to be 227 patients.

Sample technique:

Systematic random sample: Patients were selected at regular intervals from the sampling frame. The intervals are chosen to ensure an adequate sample size. A sample size of 227 from a population of 600, we selected every 600/227 = 2nd member of the sampling frame.

Study Tools:

1. Informed consent for every patient.
2. Laboratory diagnosis: HCV antibodies; blood samples were obtained from T2DM patients for HCVab (anti-HCV rapid test) in the serum. Blood samples (2ml) were taken from type2 diabetic patients put in to Vacutainer Tube (Lavender Tube) filled with (1ml) EDTA, labelled with name and date and shake gently, then put in centrifuge after that we take serum sample with dropper and put it in HCV rapid test device.
3. Questionnaires:

- **Questionnaire A**: for assessment the socio economic data guided by [8] including: age, sex, education level, marital status, no. of family members and economic level.
- **Questionnaire B** [9] includes:
- Patient history of T2DM (Duration of disease, type of treatment "oral – insulin –combined", other diseases" cardiovascular, renal, ophthalmological, orthopaedic" and life style "diet and exercise "during treatment.
- And for assessment knowledge about T2DM (Definition, causes, symptoms and complications" previous coma, peripheral neuropathy, cardiovascular complication, renal and ophthalmological").

Questionnaire C [10] includes:

- Knowledge of patient about HCV.
- Methods of transmission of HCV.
- HBV vaccination.
- Type of treatment taken for HCV if already present.
- Family history of HCV or HBV.
- Risk factors for HCV infection to be confirmed or excluded in all patients like (surgery-blood transfusion- intravenous line only -suture/stitches- endoscopy- dialysis-urinary catheter- dental procedures).

Administrative and Ethical consideration:

- An Official permission was obtained from Family Medicine Department.
- An official permission was obtained from the Internal Medicine Department.
- An official permission was obtained from the Institutional Research Board (IRB) at the Faculty of Medicine, Zagazig University.

- A signed consent was taken from all participants in this study.
- The study group was not exposed to any harm or risk.
- Confidentiality of information was assured.
- This study is done according to Helsinki guidelines.

Statistical Method:

Data analysis was performed using the software SPSS (Statistical Package for the Social Sciences) version 20. Quantitative variables were described using their means and standard deviations (Mean ± SD).

Categorical variables were described using their absolute frequencies and to compare the proportion of categorical data, Chi square test and Fisher exact test were used when appropriate.

Kolmogor¬ov-Smirnov (distribution-type) and Levene (homogeneity of variances) tests were used to verify assumptions for use in parametric tests.

To compare means of two groups, independent sample t test was used when appropriate.

Nonparametric test (Mann Whitney) was used to compare means when data was not normally distributed and to compare medians in categorical data.

ROC curve analysis was used to assess the best cutoff of studied parameters.

The level statistical significance was set at 5% (P-value<0.05). Highly significant difference was present if P-value ≤0.001.

RESULTS

The result of the study was that the prevalence of HCV antibodies among T2DM patients attending the out-patient clinic of Internal Medicine Department at Zagazig University Hospitals, Sharkia Governorate is 31.3 % (71 T2DM patients out of 227 patients enrolled in the study have HCVab) **(Table 1)**.

The prevalence is statistically higher in males (P-value = 0.016). The prevalence also is statistically higher in older age groups (P-value= 0.005) with the age range between 27 – 85years. There are non-significant differences between residence, order in family, social class, number of brothers and HCVab sero-positives as shown in **(Table 2)**.

There are significant differences between HCVab seropositive, sero-negative patients and their family history of HCV (relevant more present among HCVab seropositive cases) (P-value <0.001), risk factors (blood transfusion, more significant high in HCVab seropositive cases) (P-value <0.001) and knowledge about method of transmission (more prevalent with inadequate knowledge in HCVab seropositive cases) (P-value=0.022) **(Table 3)**.

There are significant differences between HCVab sero-positive, sero-negative patients and years of diagnosis of T2DM (more than 10 years more significant increase in infection) (P-value=0.026), comorbid disease (arthritis and cardiac disease are risk factors for infection while hypertension appears to be less) (P-value=0.003), medication (HCVab seropositive more prevalent in T2DM patients on insulin use) (P-value=0.026), family history of DM (irrelevant) (P-value <0.001) and drug on time (more significant increase occurrence of HCVab among patients take drug on time) (P-value=0.031) as shown in **(Table 4)**.

Table (1) Serology of studied participants:

Serology	T2DM patients N= 227	
	N	(%)
HCV:		
Negative	156	(68.7)
Positive	71	(31.3)

Table (2): Relation between HCVab sero-positive, sero-negative patients and their socio-demographic characteristics:

Items	HCVab sero- negative	HCVab sero- positive	Test	P-value
	N = 156 (%)	N=71 (%)		
Gender:				
Male	41 (26.3)	30 (42.3)	5.79∞	0.016
Female	115 (73.7)	41 (57.5)		(S)
Residence:				
Rural	139 (89.1)	58 (81.7)	2.337∞	0.126
Urban	17 (10.9)	13 (18.3)		(NS)
Order				
First	25 (16)	21 (29.6)		
Middle	99 (63.5)	37 (52.1)	5.59∞	0.061
Last	32 (20.5)	13 (18.3)		(NS)
Social class:				
Very low	4 (2.6)	5 (7)		
Low	101 (64.7)	46 (64.8)	3.137∞	0.371
Middle	48 (30.8)	18 (25.4)		(NS)
High	3 (1.9)	2 (2.8)		
Age				
Mean ± SD	53.18 ± 10.82	57.37 ± 9.44	-2.808¥	0.005
Range	25 – 76	27 – 85		(S)
Brothers:				
Median	5	5	-0.776§	0.438
Range	2 - 10	0 – 10		(NS)

∞ Chi square test.

¥ Independent sample t test.

§ Mann Whitney test.

Table (3) Relation between HCVab sero-positive, sero-negative patients and their family history of HCV&HBV, HBV vaccination and Knowledge about transmission:

Items	HCVab sero- negative	HCVab sero-positive	X^2	P-value
	N = 156(%)	N = 71(%)		
Family history (HCV):				
Irrelevant	125 (80.1)	38 (53.5)	17.062	<0.001
Relevant	31 (19.9)	33 (46.5)		(HS)
Family history (HBV)				
Irrelevant	154 (98.7)	71 (100)	Fisher	1
Relevant	2 (1.3)	0 (0)		(NS)
HBV vaccination:				
No	142 (91)	63 (88.7)	0.293	0.588
Yes	14 (9)	8 (11.3)		(NS)
Risk factors:				
Major surgery	65 (41.7)	30 (42.3)		
Blood transfusion	7 (4.5)	20 (28.2)∞		
IV route only	30 (19.2) ∞	4 (5.6)	33.11	<0.001
Minor surgery	3 (1.9)	0 (0)		(HS)
Endoscopy	6 (3.8)	4 (5.6)		
Urinary catheter	2 (0.6)	0 (0)		
Dental procedure	44 (28.2) ∞	13 (18.3)		
Knowledge about transmission:				
Inadequate	69 (44.2)	43 (60.6)	5.207	0.022
Adequate	87 (55.8)	28 (39.4)		(S)

∞ Chi square test.

Table (4) Relation between HCVab sero-positive, sero-negative patients and their diabetes related characteristics:

Items	HCVab sero- negative	HCVab sero- positive	X^2	P-value
	N = 156(%)	N = 71(%)		
Years of diagnosis:				
Less than 5 years	62 (39.7)	16 (22.5)		
5 to 10 years	43 (27.6)	22 (31)	6.911	0.026
More than 10 years	51 (32.7)	33 (46.5)∞		(S)
Current medications:				
Oral hypoglycemic	97 (62.2)	32 (45.1)		
Insulin	57 (36.5)	39 (54.9) ∞	7.326	0.026
Both	2 (1.3)	0 (0)		(S)
Comorbidity:				
Absent	60 (38.5)	25 (35.2)	0.220	0.639
Present	96 (61.5)	46 (64.8)		(NS)
Comorbid disease:				
Eye disease	16 (16.7)	8 (17.4)		
Hypertension	62 (64.6)	20 (43.5)∞	15.871	0.003
Arthritis	9 (9.4)	10 (21.7) ∞		(S)
Cardiac disease	2 (2.1)	7 (15.2) ∞		
Kidney disease	7 (7.3)	1 (2.2)		
Family history of DM:				
Irrelevant	41 (26.3)	37 (52.1) ∞	14.434	<0.001
Relevant	115 (73.7)	34 (47.9)		(HS)
Drugs on time				
No	7 (4.5)	0 (0)		
Sometimes	30 (19.2)	7 (9.9) ∞	6.977	0.031
Yes	119 (76.3)	64 (90.1) ∞		(S)
Forget medications:				
Never	96 (61.5)	54 (76.1)		
Once	27 (17.3)	8 (11.3)	4.606	0.100
Twice	33 (21.2)	9 (12.7)		(NS)
Extradoses:				
Never	117 (75)	45 (63.4)		
Once	32 (20.5)	22 (31)	3.305	0.192
Twice	7 (4.5)	4 (5.6)		(NS)

∞ Chi square test.

DISSCUSION

HCV and T2DM are prevalent diseases worldwide with mutual association, significant morbidity and mortality [11]. In the past, it has been observed that both diseases have a high correlation that might be due to the abnormal conditions of the liver. But the mechanism of the prevalence of diabetes in patients with chronic HCV infection still remains unclear [12]. It is unclear whether both conditions are the result of an underlying susceptibility or whether one influences the development of the other [13].

The prevalence of HCVab in T2DM patients (31.3%) was close to **Nasir et al (2017)** in which 33.77% of T2DM patients were positive for HCVab when compared to those with good glycemic control. It is lower than **Amin et al (2015)** in which 38.7 % of T2DM patients had positive HCV antibody test and **Mashahit and Ibrahim (2018)** revealed that HCVab prevalence among general population in Egypt ranges from 10 to 17%. But it is higher than **Laloo et al (2015**) done in India that found that 5.7% of T2DM patients had positive HCVab.

The study reported that HCVab prevalence is statistically significant in HCVab sero-positive T2DM males. That is in agreement with **Thrift et al (2017)** that approved that HCVab prevalence is higher in males than females. And is against **Atif et al (2017)** which revealed that diabetic females had a higher prevalence for HCVab when compared to diabetic males and **Ali et al (2015)** in which majority of cases positive for HCVab were females (63: 78%).

The study stated that HCVab prevalence is statistically significant in HCVab sero-positive cases with age (27-85years old). This is in agreement with **Shiao et al (2017)** in which patients with metabolic syndrome aged 40 years old or older had higher prevalence for HCVab. Also **World Bank (2018)** reporting that more than one in the five Egyptians age 50-59 are a carrier of Hepatitis C. But in contrast to **Ali et al (2015)**in which the majority of the HCVab positive respondents belonged to younger age group of 21 - 30 years (39%) followed by 31 - 40 years (34.3%).

The study found that HCVab prevalence is statistically significant in HCVab sero-positive T2DM patients with relevant family history for HCV. This is in agreement with **Badr et al (2016)** done on patients have clinical manifestation of liver cell failure or exposed to HCV transmission risk factors found that 71% of them had relevant family history of HCV. Also **Ali et al (2015**) reported that 60.7% males and 37.5% females HCVab positive cases had positive family history of HCV.

The study revealed that HCVab prevalence is statistically significant in HCVab sero-positive T2DM patients who were diagnosed as T2DM patients for more than 10 years (more than 10 years more significant increase in infection), medication (HCVab sero-positive more prevalent in T2DM patients on insulin use). This is nearly in agreement with **Ba-Essa et al (2016)** that reported that DM duration of >5 years increased the probability of HCV risk to 3.7 fold while insulin users were 3.2 times more likely to have HCV infection.

In contrast to **Ni et al (2012)** in which there is no significant association between duration of T2DM and HCV; showing that chronicity of DM is not a predisposing factor for HCV infection and it may be the hepatitis C infection itself leading to the development of diabetes through an uncertain mechanism.

Also in **Farshadpour et al (2018)** there was no difference between HCV-seropositive and HCV-seronegative diabetic patients in terms of medical techniques and hospital admissions but the duration of diabetes, type of treatment, severity of liver diseases, and level of liver enzymes among diabetic patients affect TG, TCH, ALT, and AST levels between the HCV-seropositive and the HCV-seronegative diabetic patients.

CONCLUSION

T2DM and HCV are two highly prevalent diseases in Egypt. In this study; the prevalence of HCVab in T2DM patients is 33.1%. About one third of T2DM patients were supposed to HCV.

Positive family history for HCV in majority of HCVab sero-positive cases

indicates role of intra-familial contact in HCV transmission.

Also routes of transmission like blood transfusion, intravenous line only, suture/stitches and endoscopy are a major risk factor as most of participants undergo surgical operation, blood transmission. That indicates the indirect role of T2DM in increasing morbidity; as ESRD, CVD or diabetic retinopathy that makes T2DM patients more susceptible to these major risk factor and thus exposed to HCV transmission.

RECOMMENDATION

We recommend:

- Health educational programs about HCV infection and how to be transmitted especially among T2DM patients.
- Other studies on a large scale must be done in different governorates in Egypt to measure the prevalence of HCV among T2DM patients.
- Guiding T2DM patients who infected with HCV for earlier adequate therapy to prevent complications and encourage those who aren't infected to be vaccinated against HBV and to be tested for HCV to be detected as early as possible.

LIMITATIONS

The study participants were taken from a tertiary hospital only which is not a good representation of the community and carry some sort of selection bias.

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