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The Screening of Diabetes, Obesity, and Hypertension Risks Associated with Hepatitis C Within the Egyptian Population in a Community Pharmacy Setting

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Abstract: *Background:* Diabetes and hypertension have been identified as risk factors for HCV complications in previous studies. This has sparked the interest in the field of prevention by identifying at-risk individuals and increasing investments for screening among pharmacists. The aim of this study was to screen for risk factors, including age, gender, BMI, hypertension, diabetes, and obesity, in Egyptian patients with HCV. *Methods:* A prospective cross-sectional study was carried out from September 2018 to February 2019, with a total of 1,959 medical records collected. By comparing the patients' characteristics, variables related to metabolic risk, and body composition measurements, regression models have been established to determine any confounding factors. *Results:* The prevalence of HCV antibody was 41.0% in men and 59.0% in women. Among the variables included in the regression analysis, age, BMI, and uncontrolled hypertension were found to have statistically significant associations with diabetes in HCV positive cases ($p < 0.001$). HCV patients ≥ 40 years old with high BMI were found to have significant associations with both, diabetes and hypertension ($p < 0.001$). Hypertensive HCV patients were found to have significant associations with gender, age ≥ 40, and DM ($p < 0.001$). *Conclusion:* HCV infection and metabolic disorders have a closed cycle relationship. Reducing the complications of DM has a promising prospective of limiting the complications of HCV.

Keywords: Hepatitis C virus; Diabetes; Obesity; Hypertension

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1. Background

Pharmacists play an essential role in screening for diabetes mellites (DM) and cardiovascular risk factors. Their involvement in this facet is beneficial to patient education and disease management [1,2]. Pharmacist-led health screening brings about great opportunities to potentially engage patients who may be less likely to gain access to physicians, including elderly patients and those from lower socio-economic background [3]. Most research on hepatitis C focuses on its detection, diagnosis, and treatment. However, this research focuses on the metabolic and hypertension risks associated with hepatitis C infection within the Egyptian population. Hepatitis C infection is considered as a major public health issue in Egypt [4]. Egypt was found to have the most elevated recorded predominance of hepatitis C virus (HCV) in the world [5,6]. Its annual incidence rate is between 2 and 6 per 1,000 cases, with 170,000 new cases being added each year [4]. Despite the fact that its mortality will continue to rise over the next 20 years, successful therapeutic strategies may escalate its eradication within 15 to 20 years [6]. Therefore, Egypt has launched an ambitious new nationwide treatment program in 2014 [7]. The Egyptian national HCV treatment program is considered one of the foremost fruitful, compelling, and promising public health programs [8]. Chronic hepatitis C is the major cause of cirrhosis and hepatocellular carcinoma. Hepatitis C is characterized as a slowly progressive disease, which implies that cirrhosis may occur 20 to 30 years after infection [9]. The primary host cells for HCV are the hepatocytes. Viral entry into hepatocytes occurs following its binding to low-density lipoprotein receptors. Once internalized, HCV interferes with the host lipid metabolism for its replication and assembly, which consequently leads to hepatic steatosis. Hepatic steatosis is a condition in which there is excessive accumulation of triglycerides inside the hepatocytes. Strong epidemiological, biochemical, and therapeutic evidence implicate insulin resistance as the main pathophysiological key mechanism leading to hepatic steatosis. Hepatic steatosis is brought about by a combination of host and viral factors [10]. Its host factors include metabolic syndromes, such as obesity and type 2 diabetes mellitus (T2DM), hypertension, alcohol abuse, as well as medication use; its hereditary factors include interleukin 28B polymorphism. Gene mutation and viral genotype are also the risk factors of hepatic steatosis (genotype 3 primarily causes steatosis) [10]. It is important to determine the modifiable risk factors that contribute to HCV progression as they may be useful to guide treatment approaches and for overall disease management. Obesity and diabetes have been linked to the progression of cirrhosis and hepatic fibrosis [8]. Recently, many studies have suggested that chronic hepatitis C (CHC) infection is associated with T2DM; however, the association between CHC and T2DM is not consistent across all studies [11]. A study conducted in France detailed that the frequency of HCV is significantly related to age [12]. Previous studies have revealed that HCV infection may not only resist the course of antiviral treatment but also promote the progression of fibrosis due to the increased proficiency of viral replication via lipid buildup in cells [11]. Lessening in complications from T2DM that follows effective antiviral treatment has been documented in later clinical trials [13]. The current study points to target high risk HCV Egyptian patients with metabolic disorders, including diabetes, obesity, hypertension, age, and gender, as well as determine the potential risk factors associated with hepatitis C patients and the impact of different screening methods for identifying and treating individuals at high risk.

2. Methods

2.1. Subject

This study was a cross-sectional study, in which the medical records of 1,959 HCV positive patients obtained from the "hepatic virus section" in a university hospital from September 2018 to February 2019 were reviewed. The sample included patients aged from 19 to 94 years old and both, male and female patients. Children and HIV patients were excluded.

2.2. Study data

For obesity, body mass index (BMI) was calculated by dividing body weight in kilograms with the square of height in meters (kg/m^2); the BMI of the patients was categorized into three categories: normal (BMI < 25), overweight (BMI = 25 to < 30), and obese (BMI ≥ 30).

For hypertension, the average of three readings was calculated. Hypertensive patients were defined as patients having an average systolic of more than or equal to 130 mmHg or an average diastolic of more than or equal to 90 mmHg. Those who are using antihypertensives were also considered hypertensive.

In terms of HCV testing, HCV antibody (HCV-Ab) test was used to determine HCV antibodies. Negative ELISA samples were excluded, but positive ELISA samples were retested for HCV antibodies using a more specific assay and further tested by using quantitative real-time PCR to detect HCV-RNA. Those with positive sera for HCV antibodies through ELISA and with positive PCR-RNA were considered as having chronic HCV infection.

2.3. Study design

The relationships between different parameters and risk factors in 1,959 HCV positive patients were studied. The relationships between DM, BMI, age, and hypertension (HTN) with the rest of the parameters and risk factors in HCV positive patients were studied. The study protocol was approved by the university hospital, and the patients signed the informed consent form before initiating the study. All procedures contributing to this study complied with the ethical standards of the Scientific Ethics Committee Board at the School of Pharmacy in Damanhour University.

2.4. Statistical analysis

The data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp.). The qualitative data were described using numbers and percentages. Kolmogorov-Smirnov test was used to verify the normality of distribution. The quantitative data were described using range (minimum and maximum), mean, standard deviation, and median. The results were judged at a significance level of 5%.

The tests used were Chi-square test, Fisher's exact test or Monte-Carlo correction, Mann-Whitney test, Kruskal-Wallis test, and the post hoc test (Dunn's multiple comparison test) for pairwise comparisons. A series of univariate and multivariate logistic regression analyses were performed to investigate the factors associated with HCV infection and to detect the most independent or affecting factor among DM, HTN, and BMI.

3. Results

The final eligible study sample comprised of 1,959 patients in the age group of 18 to 95 years old.

3.1. Prevalence of diabetes mellitus in HCV positive cases

As shown in **Table 1**, there were 1,661 (84.4%) patients with normal blood glucose level (BGL) and 71 (3.6%) patients with abnormal BGL, which were considered as new diabetic cases. Among the patients who have a history of diabetes, there were 99 (5.5%) patients with well-controlled DM, and 128 (6.5%) patients with uncontrolled DM. The infection rates were similar between male and female patients, and there was no statistically significant difference ($p = 0.093$). Among the variables included in the regression analysis, age, BMI, and uncontrolled HTN were statistically significant ($p < 0.001$). After the adjustment of demographic and HCV risk factors, it was found that HCV is significantly associated with several subgroups: age ≥ 40 years ($p = 0.001$), BMI ≥ 30 kg/m^2 ($p = 0.022$), and HTN ($p < 0.001$), as shown in **Table 2**.

Table 1. Relationship between DM and different parameters in HCV positive cases (n = 1,959)

	Normal (n = 1661)		DM						Test of sig.	*p*
			New DM (n = 71)		Controlled DM (n = 99)		Uncontrolled DM (n = 128)			
	Number	%	Number	%	Number	%	Number	%		
Gender										
Male	694	41.8	31	43.7	37	37.4	41	32.0	χ^2 = 5.423	0.143
Female	967	58.2	40	56.3	62	62.6	87	68.0		
Age (years)										
< 40	273[a]	16.4	2[b]	2.8	6[b]	6.1	2[b]	1.6	χ^2 = 35.913*	< 0.001*
≥ 40	1388[a]	83.6	69[b]	97.2	93[b]	93.9	126[b]	98.4		
Min. – Max.	19.0 – 93.0		30.0 – 79.0		26.0 – 94.0		25.0 – 77.0		H = 78.833*	< 0.001*
Mean ± SD	53.08[b] ± 13.59		60.76[a] ± 9.67		60.11[a] ± 11.36		59.88[a] ± 8.53			
Median	54.0		61.0		62.0		61.50			
BMI (kg/m^2)										
18.5-24.9 (Normal)	435[a]	26.2	21[a]	29.6	12[b]	12.1	14[b]	10.9	χ^2 = 40.488*	< 0.001*
25-29.9 (Overweight)	512[a]	30.8	19[a]	26.8	25[a]	25.3	31[a]	24.2		
≥ 30 (Obese)	714[a]	43.0	31[a]	43.7	62[b]	62.6	83[b]	64.8		
< 30	947[a]	57.0	40[a]	56.3	37[b]	37.4	45[b]	35.2	χ^2 = 35.359*	< 0.001*
≥ 30	714[a]	43.0	31[a]	43.7	62[b]	62.6	83[b]	64.8		
Min. – Max.	16.96 – 64.84		19.72 – 54.50		20.06 – 56.89		16.41 – 58.59		H = 34.512*	< 0.001*
Mean ± SD	29.74[b] ± 6.59		30.38[b] ± 7.42		32.26[a] ± 6.62		32.17[a] ± 6.73			
Median	28.69		28.41		32.45		32.01			
Systolic										
< 130	1010[a]	60.8	21[b]	29.6	28[b]	28.3	44[b]	34.4	χ^2 = 90.917*	< 0.001*
≥ 130	651[a]	39.2	50[b]	70.4	71[b]	71.7	84[b]	65.6		
Min. – Max.	80.0 – 210.0		80.0 – 220.0		90.0 – 206.0		90.0 – 190.0			
Mean ± SD	124.74[b] ±18.33		137.11[a] ± 23.64		135.70[a] ± 20.98		133.87[a] ± 20.02		H = 80.889*	< 0.001*
Median	120.0		130.0		130.0		130.0			
Diastolic										
< 80	492[a]	29.6	13[b]	18.3	15[b]	15.2	27[b]	21.1	χ^2 = 16.629*	0.001*
≥ 80	1169[a]	70.4	58[b]	81.7	84[b]	84.8	101[b]	78.9		
Min. – Max.	50.0 – 140.0		50.0 – 140.0		60.0 – 120.0		56.0 – 120.0			
Mean ± SD.	80.81[b] ± 11.51		86.34[a] ± 13.86		86.67[a] ± 11.95		84.15[a] ± 12.70		H = 46.767*	0.001*
Median	80.0		90.0		90.0		80.0			
HTN										
Normal	1462[a]	88.0	69[b]	97.2	30[c]	30.3	66[d]	51.6	χ^2 = 325.072*	< 0.001*
Hyper	199[a]	12.0	2[b]	2.8	69[c]	69.7	62[d]	48.4		

Note: [a] / [b] / [c] / [d]: means with common alphabets are not significant (i.e., means with different alphabets are significant); χ^2: chi-square test; H: H value in Kruskal Wallis test; pairwise comparison between two groups was done using the post hoc test (Dunn's multiple comparison test); *p*: *p* value for comparing between the four categories; *: statistically significant at $p \leq 0.05$

Table 2. Univariate and multivariate analyses of factors affecting different parameters in HCV positive cases (n = 1,959)

	Univariate		#Multivariate	
	p	**OR (95% CI)**	***p***	**OR (95% CI)**
Diabetes affecting studied parameters				
Age ≥ 40 (years)	< 0.001*	5.538 (3.141 – 9.765)	0.001*	3.073 (1.584 – 5.960)
BMI ≥ 30 (kg/m^2)	< 0.001*	1.983 (1.553 – 2.532)	0.022*	1.369 (1.046 – 1.791)
Systolic (≥ 130 mmHg)	< 0.001*	3.342 (2.588 – 4.315)	< 0.001*	2.116 (1.505 – 2.976)
Diastolic (≥ 80 mmHg)	< 0.001*	1.845 (1.364 – 2.497)	0.204	0.778 (0.528 – 1.147)
HTN	< 0.001*	5.922 (4.511 – 7.775)	< 0.001*	3.910 (2.909 – 5.254)
BMI ≥ 30 affecting studied parameters				
Gender	< 0.001*	5.058 (4.135 – 6.188)	< 0.001*	5.158 (4.190 – 6.351)
Age ≥ 40 (years)	< 0.001*	1.722 (1.323 – 2.241)	0.009*	1.480 (1.103 – 1.985)
Systolic (≥ 130 mmHg)	< 0.001*	1.803 (1.505 – 2.160)	0.067	1.250 (0.985 – 1.587)
Diastolic (≥ 80 mmHg)	< 0.001*	1.606 (1.311 – 1.966)	0.006*	1.419 (1.106 – 1.820)
DM	< 0.001*	1.913 (1.489 – 2.458)	0.014*	1.436 (1.076 – 1.918)
HTN	< 0.001*	2.675 (2.090 – 3.423)	0.001*	1.627 (1.218 – 2.175)
HTN affecting studied parameters				
Gender	< 0.001*	2.135 (1.643 – 2.774)	< 0.001*	2.252 (1.686 – 3.007)
Age ≥ 40 (years)	< 0.001*	11.148 (4.921 – 25.256)	< 0.001*	4.640 (1.985 – 10.846)
Systolic (≥ 130 mmHg)	< 0.001*	8.096 (6.014 – 10.900)	< 0.001*	5.022 (3.529 – 7.146)
Diastolic (≥ 80 mmHg)	< 0.001*	4.342 (2.972 – 6.344)	0.096	1.479 (0.932 – 2.347)
DM	< 0.001*	5.922 (4.511 – 7.775)	< 0.001*	4.183 (3.109 – 5.629)

Note: OR: odds ratio; CI: confidence interval; #: all variables with $p < 0.05$ were included in the multivariate; *: statistically significant at $p \leq 0.05$

3.2. Based on BMI variation in HCV positive cases

From **Table 3**, based on the BMI classification, there were 482 HCV positive cases (24.6%) with normal weight (BMI = 18.5-24.9), 587 overweight cases (BMI = 25-29.9), and 890 (45.4%) obese cases (BMI of 30 or greater). Among the variables included in the analysis, gender and HTN were statistically significant ($p < 0.001$). From the univariate and multivariate analyses, it was found that HCV is significantly associated with several subgroups: age over 40 years old ($p = 0.009$) and DM ($p = 0.014$), as shown in **Table 2**.

Table 3. Relationship between BMI and different parameters in HCV positive cases (n = 1,959)

	BMI (kg/m^2)						Test of sig.	*p*
	Normal BMI = 18.5-24.9 (n = 482)		**Overweight BMI = 25-29.9 (n = 587)**		**Obese BMI > 30 (n = 890)**			
	Number	**%**	**Number**	**%**	**Number**	**%**		
Gender								
Male	316[a]	65.6	299[b]	50.9	188[c]	21.1	χ^2 = 289.529*	< 0.001*
Female	166[a]	34.4	288[b]	49.1	702[c]	78.9		
Age (years)								
< 40	90[a]	18.7	96[a]	16.4	97[b]	10.9	χ^2 = 17.756*	< 0.001*
≥ 40	392[a]	81.3	491[a]	83.6	793[b]	89.1		
Min. – Max.	19.0 – 87.0		19.0 – 94.0		20.0 – 93.0			
Mean ± SD	53.79 ± 14.94		53.79 ± 13.93		54.59 ± 11.91		H = 0.531	0.767
Median	56.0		54.0		55.0			
Random blood sugar								
Min. – Max.	72.0 – 570.0		71.0 – 568.0		71.0 – 557.0		H = 26.286*	< 0.001*
Mean ± SD	128.53[b] ± 68.23		131.90[b] ± 65.35		143.52[a] ± 77.73			
Median	110.0		113.0		117.0			
Systolic								
< 130	327[a]	67.8	345[b]	58.8	431[c]	48.4	χ^2 = 49.983*	< 0.001*
≥ 130	155[a]	32.2	242[b]	41.2	459[c]	51.6		
Min. – Max.	80.0 – 220.0		80.0 – 210.0		80.0 – 206.0			
Mean ± SD	121.70[c] ± 19.53		125.96[b] ± 19.17		129.11[a] ± 18.47		H = 62.591*	< 0.001*
Median	120.0		120.0		130.0			
Diastolic								
< 80	183[a]	38.0	161[b]	27.4	203[c]	22.8	χ^2 = 35.797*	< 0.001*
≥ 80	299[a]	62.0	426[b]	72.6	687[c]	77.2		
Min. – Max.	50.0 – 140.0		50.0 – 140.0		50.0 – 140.0			
Mean ± SD	78.56[c] ± 11.63		81.14[b] ± 11.71		83.38[a] ± 11.66		H = 59.736*	< 0.001*
Median	80.0		80.0		80.0			
DM								
Normal	435[a]	90.2	512[a]	87.2	714[b]	80.2		
New DM	21[a]	4.4	19[a]	3.2	31[a]	3.5	χ^2 = 40.488*	< 0.001*
Controlled DM	12[a]	2.5	25[a]	4.3	62[b]	7.0		
Uncontrolled DM	14[a]	2.9	31[a]	5.3	83[b]	9.3		
Normal	435[a]	90.2	512[a]	87.2	714[b]	80.2	χ^2 = 28.213*	< 0.001*
Diabetic	47[a]	9.8	75[a]	12.8	176[b]	19.8		

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	BMI (kg/m^2)							
	Normal BMI = 18.5-24.9 (n = 482)		Overweight BMI = 25-29.9 (n = 587)		Obese BMI > 30 (n = 890)		Test of sig.	*p*
	Number	%	Number	%	Number	%		
HTN								
Normal	444[a]	92.1	510[b]	86.9	673[c]	75.6	χ^2 = 69.199*	< 0.001*
Hyper	38[a]	7.9	77[b]	13.1	217[c]	24.4		

Note: [a] / [b] / [c]: means with common alphabets are not significant (i.e., means with different alphabets are significant); χ^2: chi-square test; H: H value in Kruskal-Wallis test; pairwise comparison between two groups was done using the post hoc test (Dunn's multiple comparison test); *p*: *p* value for comparing between the three categories; *: statistically significant at $p \leq 0.05$

3.3. Based on age variation in HCV positive cases

With age more than or equal to 40 years old, the prevalence of HCV increases, as shown in **Table 4**. A total of 1,676 cases (85.6%) were over or equal to 40 years old. Based on the relationships between different ages and all the included parameters in HCV positive cases, all the parameters were statistically significant, with $p < 0.001$, except for gender, which was not statistically significant ($p = 0.239$).

Table 4. Relationship between age and different parameters in HCV positive cases (n = 1,959)

	Age (years)				Test of sig.	*p*
	< 40 (n = 283)		≥ 40 (n = 1,676)			
	Number	%	Number	%		
Gender						
Male	107	37.8	696	41.5	χ^2 = 1.384	0.239
Female	176	62.2	980	58.5		
BMI (kg/m^2)						
Normal	90	31.8	392	23.4		
Overweight	96	33.9	491	29.3	χ^2 =17.756*	< 0.001*
Obese	97	34.3	793	47.3		
< 30	186	65.7	883	52.7	χ^2 = 16.605*	< 0.001*
≥ 30	97	34.3	793	47.3		
Min. – Max.	19.0 – 39.0		40.0 – 94.0		U = 194612.0*	< 0.001*
Mean ± SD	31.50 ± 5.63		57.98 ± 10.04			
Median	33.0		58.0			
DM						
Normal	273	96.5	1388	82.8		
New DM	2	0.7	69	4.1	χ^2 = 35.913*	< 0.001*
Controlled DM	6	2.1	93	5.5		
Uncontrolled DM	2	0.7	126	7.5		
Normal	273	96.5	1388	82.8	U = 154659.50*	< 0.001*
Diabetic	10	3.5	288	17.2		

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	Age (years)				Test of sig.	*p*
	< 40 (n = 283)		≥ 40 (n = 1,676)			
	Number	%	Number	%		
HTN						
Normal	277	97.9	1350	80.5	$\chi^2 = 51.667$*	< 0.001*
Hyper	6	2.1	326	19.5		

Note: χ^2: chi-square test; U: Mann-Whitney test; *p*: *p* value for comparing between the two categories; *: statistically significant at $p \leq 0.05$

3.4. Prevalence of hypertension in HCV positive cases

The average prevalence of HTN in HCV patients is 26.8% in men and 73.2% in women ($p < 0.001$). The prevalence of HTN in cases over 40 years old is 98.2% ($p < 0.001$). The prevalence of HTN among individuals with obesity is 65.4%. The estimated prevalence of DM in patients with HTN is 40.1% ($p < 0.001$), as shown in **Table 5**.

Table 5. Relationship between HTN and different parameters in HCV positive cases (n = 1,959)

	HTN				Test of sig.	*p*
	Normal (n = 1,627)		Hyper (n = 332)			
	Number	%	Number	%		
Gender						
Male	714	43.9	89	26.8	$\chi^2 = 33.245$*	< 0.001*
Female	913	56.1	243	73.2		
Age (years)						
< 40	277	17.0	6	1.8	$\chi^2 = 51.667$*	< 0.001*
≥ 40	1350	83.0	326	98.2		
Min. – Max.	19.0 – 93.0		26.0 – 94.0			
Mean ± SD	52.50 ± 13.27		62.26 ± 10.28		U = 153379.50	< 0.001*
Median	53.0		63.0			
BMI (kg/m^2)						
Normal	444	27.3	38	11.4		
Overweight	510	31.3	77	23.2	$\chi^2 = 69.199$*	< 0.001*
Obese	673	41.4	217	65.4		
< 30	954	58.6	115	34.6	$\chi^2 = 64.048$*	< 0.001*
≥ 30	673	41.4	217	65.4		
Min. – Max.	16.41 – 64.84		17.96 – 57.16			
Mean ± SD	29.40 ± 6.38		33.22 ± 7.16		U = 183448.50*	< 0.001*
Median	28.39		32.89			
DM						
Normal	1462	89.9	199	59.9		
New DM	69	4.2	2	0.6	$\chi^2 = 325.072$*	< 0.001*
Controlled DM	30	1.8	69	20.8		
Uncontrolled DM	66	4.1	62	18.7		

Note: χ^2: chi-square test; U: Mann-Whitney test; *p*: *p* value for comparing between the two categories; *: statistically significant at $p \leq 0.05$

4. Discussion

With a sample size of 1,959 patients, this study illuminates the effect of cofounding factors, such as HTN, DM, BMI, age, and gender, in patients with HCV infection. Illustrating each of these points depends on a multivariate analysis for different parameters and the risk factors in HCV positive patients. After analyzing the results, among those with HCV infection, female patients were found to be more (1,156 patients, 59%) than male patients (803 patients, 41%); 85.6% of the infected patients were aged ≥ 40 years old; 45.5% were obese with a BMI ≥ 30 (kg/m^2); 43.7% were with uncontrolled blood pressure, in which the systolic blood pressure ≥ 130 mmHg; 72.1% were found to have diastolic blood pressure ≥ 80 mmHg.

In this study, it was found that in all patients with chronic HCV, being ≥ 40 years old and having a BMI of ≥ 30 (kg/m^2) as well as a high systolic blood pressure of ≥ 130 mmHg are all independent risk factors for type 2 diabetes mellitus (T2DM). These findings suggest that ageing, being obese, and having high uncontrolled blood pressure along with HCV infection will increase the risk of developing glucose abnormalities, including anomalies in carbohydrate metabolism, insulin resistance, and metabolic clutters, which may progress into T2DM [14].

Several studies have contrived several explanations for this hypothesis – the increased risk of developing DM in HCV infected patients. According to Abdelaziz and other researchers [1], diabetic patients may become infected as a result of contaminated injections or nosocomial transmission, although this notion has been debunked in view of the widespread application of universal precautions in hospitals. Other possible mechanisms include the impairment of glucose metabolism and reduction in glucose uptake by cells as a result of the progression of liver fibrosis and cirrhosis as common complications of being HCV positive [14]. Cirrhosis itself is considered diabetogenic. On the other hand, diabetes can worsen the outcome of hepatitis C, which includes increasing the risk for cirrhosis and hepatocellular carcinoma (HCC) [16,17].

Another study has suggested that the eradication of HCV in T2DM patients with direct-acting antiviral (DAA) therapy improves glycemic control, lowers glycated hemoglobin (HbA1c), and lowers insulin requirements [18].

In regard to other factors linking diabetes and HCV, females, as mentioned above, have higher rate than men in this study and another study [1]. However, other studies have found that hepatitis C is more common in men than in women, and that male patients are more associated with its disease progression to fibrosis and cirrhosis [16].

The occurrence and recurrence of HCC are high among patients with chronic HCV infection, obesity, and heavy alcohol intake. Furthermore, obesity-related nonalcoholic fatty liver disease (NAFLD) might exacerbate liver inflammation or lead to other obesity-related disorders [19,20]. In this study, one of the interesting findings was the impact of BMI. The multivariate analysis revealed that having a BMI of ≥ 30 (kg/m^2) affects different parameters in HCV positive patients. It was found that the incidence of HCV infection is higher among those obese, aged ≥ 40 years, diabetic with blood glucose ≥ 200 mg/dL, and with uncontrolled blood pressure (diastolic blood pressure ≥ 80 mmHg).

Based on a study conducted by Ali-Eldin and other researchers [21], free fatty acid and cytokine secretion induced by adipose tissue dysfunction may contribute to liver steatosis and the induction of inflammation, reporting a positive correlation in the degree of hepatic fibrosis and hepatic affection in chronic HCV patients. Furthermore, the changes in glucose metabolism leading to insulin resistance are all associated with liver diseases. Therefore, changes in the hosts' lipid metabolism due to chronic HCV with increasing viral replication may lead to steatosis and affect the efficacy of interferon-based therapy. This represents a novel target for therapeutic intervention in HCV eradication.

Another relevant aspect to consider from the multivariate analysis is the predominance of cardiovascular diseases with higher rates of morbidity and mortality, especially in hypertensive patients with systolic blood pressure of ≥ 130 mmHg and diastolic blood pressure of ≥ 80 mmHg along with a BMI

of ≥ 30 kg/m^2 [22]. This is unlike other studies that depend only on hypertension and diabetes, showing a two-fold increased risk of subclinical carotid plaques among HCV-infected individuals compared to uninfected controls, as well as an increase in the rate of peripheral artery disease. This could be attributable to the severity of liver damage or even the direct viral activity [23].

In a recent study, untreated HCV infected people have twice the risk of developing cardiovascular diseases (CVD), such as coronary artery disease, acute myocardial infarction, congestive heart failure, unstable angina, stroke, peripheral vascular disease, and even requiring revascularization procedures, compared to those who initiated treatment [24]. Therefore, there is significant benefit of HCV treatment on the incidence and risk of possible CVD events in the future [24]. Other studies have shown that co-infection with both HCV/HIV is associated with an increased risk of CVD [25,26]. Hence, compared to HIV-monoinfected patients and HIV-coinfected patients without cirrhosis, HIV/HCV-coinfected patients have the worst survival rate [27]. Concerning another study, persistent HCV replication leads to a state of systemic inflammation and immune activation, resulting in endothelial dysfunction, atherosclerosis, and an increased CVD risk [15].

5. Limitations

First, the sample size was relatively small, which may have influenced the statistical outcome. Second, individual variations among patients, such as marital status, rural residency, injections for bilharziasis, blood transfusions, acupuncture, and tattooing, were not taken into account. Third, the lack of data on the severity of liver fibrosis may have affected the judgement on some cases. Fourth, the dependence on "self-reporting" for cardiovascular diseases may have limited the number of these reports. Also, the lack of laboratory data on lipid and lipoprotein profile as well as the levels of liver enzymes without accounting for their potential elevation may have confounded the association of diabetes and cardiovascular events all together in HCV infected patients.

6. Conclusion

In light of the results of the present study, it was found that HCV infection triggers metabolic disorders, abnormalities in carbohydrate metabolism, including hyperinsulinemia, insulin resistance, and diabetes, especially type 2 diabetes mellitus, which arises from steatosis and inflammatory processes. Also, it was found that diabetes worsens the outcome of hepatitis C as it increases the risk for cirrhosis and HCC. Attempting to reduce the complications of diabetes has a promising future of limiting the symptoms of HCV infection in patients. Uncontrolled blood pressure may increase the risk for CVD, the incidence of peripheral arterial diseases, carotid plaques, endothelial dysfunction, and atherosclerosis. Therefore, a good control of blood pressure would be helpful to reducing the incidence of major CVD events. Obese patients with BMI ≥ 30 kg/m^2 and free fatty acid secretions may promote inflammation and the changing of lipid-cholesterol biosynthesis that causes fatty liver, hypercholesterolemia, and fibrosis. Controlling the patient's weight may help prevent complications associated with HCV infection, such as fibrosis and HCC.

Disclosure statement

The authors declare no conflict of interest.

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