The Missing Piece, The Screening for Diabetes ,Obesity and Hypertension Risk Factors Associated with Hepatitis C In Egyptian Population in a Community Pharmacy Setting.

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Abstract

Background: Risk factors for hepatitis C complication including diabetes and hypertension have seen in a many previous studies. This made the need for prompted interest in prevention through the identifying individuals at risk for these risk factors and increased investment in screening by pharmacist. Objectives: The aim of this study is to screen for several risk factors include (age, sex, BMI, Hypertension, diabetes and obesity) in HCV positive (1959) Egyptian patients. Setting: Prospective cross sectional study from September 2018 to February 2019. A total of 1959 medical records were collected. By comparing the patient characteristics, variables related to metabolic risk and body composition measured. Regression models were built to adjust for possible confounding factors. Results: The positive HCV antibody prevalence rate was 41.0 % in men and 59.0 % in women. The variables included in regression analysis are age, BMI, uncontrolled HTN were statistically significant ($P < 0.001$) with DM in HCV positive cases. HCV Patients with high BMI with age [?]40 (years) associated significantly with diabetes and HTN ($p<0.001$). Hypertensive HCV Egyptian patients were significantly associated with sex, age >40 and DM ($p< 0.001$). Conclusion HCV infection and metabolic disorders spin in a closed cycle relationship. Reducing the complications of DM has a promising future of limiting the complications of HCV.

Conclusion

HCV infection and metabolic disorders spin in a closed cycle relationship. Reducing the complications of DM has a promising future of limiting the complications of HCV.

Keywords: Hepatitis C virus , Diabetes , Obesity , Hypertension

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Introduction:

Pharmacistsalready have an essential role in screening for Diabetes mellites and Cardiovascular risk and their involvement has beneficial effects in patient education and disease management [1] [2]. Pharmacist-led health screening represents a great opportunity to potentially engage pharmacists with patients who may be less likely to access physicians including elderly patients, and patients from lower socio-economic status [3]. The majority of research in hepatitis C disease focused on the detection , diagnosis and treatment. However, in this research we focused on the metabatic and hypertension risk associated with hepatitis C infection in Egyptian population. Virus C is considered as a gigantic endemic therapeutic health issue in Egypt [4] . Egypt was found to have the most elevated recorded predominance of HCV in the world [5] [6]. Incidence rate is between 2 and 6 per 1000 case per year and 170,000 new cases are added each year [4] . Although mortality related to HCV infection will continue to extend over the following 20 years but, with successful therapeutic strategies it may be eliminated within 15-20 years [6]. Therefore , Egypt has propelled an ambitious new national 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 most cause of cirrhosis and hepatocellular carcinoma. Hepatitis C is characterized by being a slowly progressing liver illness, which implies that cirrhosis may happen almost 20–30 years after infection [9] . The primary host cells for HCV are hepatocytes. Viral entry into hepatocytes occurs following to 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 could be a condition in which there is excessive accumulation of triglycerides inside the hepatocytes. Strong epidemiological, biochemical, and therapeutic evidence implicate insulin resistance as the essential pathophysiological key mechanism driving to hepatic steatosis. A mixture of several host and viral factors cause hepatic steatosis[10] . First, host factors incorporate the metabolic syndromes such as obesity and type 2 diabetes mellitus (T2DM), hypertension, alcohol abuse and medication use. Second, hereditary factors as interleukin 28B polymorphism. Third facor is viral components as genotype (genotype 3 prima rily cause steatosis), and gene mutation [10] . It is very useful to distinguish modifiable risk factors that contribute to HCV progression it may guide treatment approaches and overall disease management. Impact of obesity and DM have been entangled within the progression of hepatic fibrosis and cirrhosis [8]. Recently, many studies have suggested that chronic hepatitis C virus infection (CHC) is associated with T2DM, However the association between CHC and T2DM is not consistent across all studies [11] . Another study in France detailed that HCV frequency was significantly related with age [12] . Previous studies demonstrated that HCV infection might not only resist antiviral course of treatment but also moreover advancement of fibrosis may happen which is due to expanded proficiency of viral replication by lipid accumulation in cells [11] . Lessening in complications from T2DM that follows effective antiviral treatment was detailed 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 sex then estimate the potential risk factors associated with hepatitis C patients and determine the impact of different screening methods for identifying and treating people at high risk

Subjects and Methods:

This is a cross sectional study where medical records of 1959 HCV positive patients obtained from one University Hospital "hepatic virus section" from (September 2018 to February 2019) were reviewed . Study sample: All patients in the sample aged from 19 to 94 years old. Sample included both males and females. Children and HIV patients were excluded.

Study data: For obesity, Body mass index (BMI) was calculated as the body weight in kilograms divided by the square of the height in meters (kg/m2), BMI 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 and the hypertensive patients were defined as patients having average systolic [?]130 mmHg or average diastolic [?]90 mmHg. Patients who were using antihypertensive drugs were considered hypertensive.

HCV testing protocol: HCV-Ab test was initially used to check HCV antibodies. Negative ELISA samples were excluded. Positive ELISA samples were retested for HCV antibodies using a more specific assay and further tested by quantitative real-time PCR to detect HCV-RNA. Participants with positive sera for HCV

antibodies by ELISA test and positive PCR-RNA were considered as chronic HCV infection.

Study design: We studied relationships between different patient parameters and risk factors in 1959 HCV positive patient. Relationship between DM, BMI, age and HTN with the rest of the parameters and risk factors in HCV positive patients were studied. Study protocol was approved by the University hospital and patients signed informed consent forms before starting the study.

Statistical analysis of the data: Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) . Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level.

The used tests were Chi-square , Fisher's Exact or Monte Carlo correction , Mann Whitney test , Kruskal Wallis test and Post Hoc (Dunn's multiple comparisons test) for pairwise comparisons. Regression using a series of univariate and multivariable logistic regression analyses were performed to investigate the factors associated with the HCV infection. To detect the most independent/ affecting factor for DM, HTN and BMI.

RESULT:

The final eligible study sample comprised 1959 patients in the age group 18–95 years.

1) The prevalence of diabetes mellitus in HCV positive cases:

As shown in Table (1) including 1661(84.4%) patients without abnormalities in blood glucose level (BGL) measures while 71 (3.6%) patients discovered abnormalities in their BGL considered as new diabetic cases. For patients who are with history of diabetes: 99(5.5%) patient with well controlled DM and 128(6.5%) patients with uncontrolled DM. The infection rates were similar between males and females and there was no statistically significant difference with ($p = 0.093$). The variables included in regression analysis are age, BMI, and uncontrolled HTN were statistically significant ($P < 0.001$). After adjustment of demographic and HCV risk factors, It was found that HCV was significantly associated with sub groups Age [?]40 years ($p = 0.001$), BMI [?]30 kg/m^2 (p=0.022), HTN (p<0.001) Table (5).

2) According to BMI variation in HCV positive cases:

Using classification of BMI shown in table (2) and Normal weight (BMI = 18.5–24.9). There are 482 cases (24.6%) with HCV positive result, there are 587 cases which are considered overweight (BMI= 25–29.9) and 890 Obese cases (45.4%) (BMI of 30 or greater) .The variables included in analysis are: sex, uncontrolled HTN were statistically significant ($P < 0.001$), age over 40 years old ($p = 0.009$), DM (p0.014), Table (4)

3) According to variation in age in patients with HCV positive:

It was clear that at the age which is more than 40 years old, the prevalence of HCV increases as shown in table (3) , 1676 cases (85.6%) were over 40 year old. Using the relation between all the parameters with different ages in HCV positive cases, all parameters were statistically significant with p <0.001 except sex was not statistically significant, as p was 0.239.

4) The prevalence of hypertension in HCV positive cases:

The average prevalence of HTN in HCV patients is (29.8%) 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 the participants with HTN is (40.1%, p<0.001) as shown in Table (4).

Table (1) Relation between DM and different parameters in positive HCV (n=1959)

Normal

(n=1661)

Normal

(n=1661)

DM

DM

DM

DM

DM

DM

Test of

sig.

P

New DM

(n=71)

New DM

(n=71)

Controlled DM (n=99)

Controlled DM (n=99)

Un controlled DM (n=128)

Un controlled DM (n=128)

No.

%

No.

%

No.

%

No.

%

Sex

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

19.0 – 93.0

30.0 – 79.0

30.0 – 79.0

26.0 – 94.0

26.0 – 94.0

25.0 – 77.0

25.0 – 77.0

H= 78.833[*]

<0.001[*]

Mean ± SD.

53.08[b] ± 13.59

53.08[b] ± 13.59

60.76[a] ± 9.67

60.76[a] ± 9.67

60.11[a] ± 11.36

60.11[a] ± 11.36

59.88[a] ± 8.53

59.88[a] ± 8.53

Median

54.0

54.0

61.0

61.0

62.0

62.0

61.50

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

16.96 – 64.84

19.72 – 54.50

19.72 – 54.50

20.06 – 56.89

20.06 – 56.89

16.41 – 58.59

16.41 – 58.59

H= 34.512*

<0.001*

Mean ± SD.

29.74^{b} ± 6.59

29.74^{b} ± 6.59

30.38^{b} ± 7.42

30.38^{b} ± 7.42

32.26^{a} ± 6.62

32.26^{a} ± 6.62

32.17^{a} ± 6.73

32.17^{a} ± 6.73

Median

28.69

28.69

28.41

28.41

32.45

32.45

32.01

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 – 210.0

80.0 – 220.0

80.0 – 220.0

90.0 – 206.0

90.0 – 206.0

90.0 – 190.0

90.0 – 190.0

Mean ± SD.

124.74[b]±18.33

124.74[b]±18.33

137.11[a] ±23.64

137.11[a] ±23.64

135.70[a]± 20.98

135.70[a]± 20.98

133.87[a] ± 20.02

133.87[a] ± 20.02

H= 80.889[*]

<0.001[*]

Median

120.0

120.0

130.0

130.0

130.0

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

50.0 – 140.0

50.0 – 140.0

60.0 – 120.0

60.0 – 120.0

56.0 – 120.0

56.0 – 120.0

Mean ± SD.

80.81[b] ± 11.51

80.81[b] ± 11.51

86.34[a] ± 13.86

86.34[a] ± 13.86

86.67[a] ± 11.95

86.67[a] ± 11.95

84.15[a] ± 12.70

84.15[a] ± 12.70

H= 46.767*

0.001*

Median

80.0

80.0

“90.0

“90.0

90.0

90.0

80.0

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

a,b,c,d : Means with **Common letters** are not significant (i.e. Means with **Different letters** are significant)

χ^2: Chi square test

H: H for **Kruskal Wallis test,** Pairwise comparison bet. each 2 groups was done using **Post Hoc Test (Dunn’s for multiple comparisons test)**

p: p value for comparing between the **four categories**

*: Statistically significant at p [?] 0.05

Table (2) Relation between BMI and different parameters in positive HCV (n=1959)

	BMI (kg/m²)	**BMI (kg/m²)**	**BMI (kg/m²)**	**BMI (kg/m²)**	**BMI (kg/m²)**	**BMI (kg/m²)**	**Test of sig.**	**p**
	Normal BMI = 18.5-24.9 (n=482)	**Normal BMI = 18.5-24.9 (n=482)**	**Overweight BMI = 25-29.9 (n=587)**	**Overweight BMI = 25-29.9 (n=587)**	**Obese BMI > 30 (n=890)**	**Obese BMI > 30 (n=890)**		
	No.	**%**	**No.**	**%**	**No.**	**%**		
Sex								
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 – 87.0	19.0 – 94.0	19.0 – 94.0	20.0 – 93.0	20.0 – 93.0		
Mean ± SD.	53.79 ± 14.94	53.79 ± 14.94	53.79 ± 13.93	53.79 ± 13.93	54.59 ± 11.91	54.59 ± 11.91	H= 0.531	0.767
Median	56.0	56.0	54.0	54.0	55.0	55.0		
Random blood sugar								
Min. – Max.	72.0 – 570.0	72.0 – 570.0	71.0 – 568.0	71.0 – 568.0	71.0 – 557.0	71.0 – 557.0	H= 26.286*	<0.001*
Mean ± SD.	128.53[b] ± 68.23	128.53[b] ± 68.23	131.90[b] ± 65.35	131.90[b] ± 65.35	143.52[a] ± 77.73	143.52[a] ± 77.73		
Median	110.0	110.0	113.0	113.0	117.0	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 – 220.0	80.0 – 210.0	80.0 – 210.0	80.0 – 206.0	80.0 – 206.0		
Mean ± SD.	121.70[c] ± 19.53	121.70[c] ± 19.53	125.96[b] ± 19.17	125.96[b] ± 19.17	129.11[a] ± 18.47	129.11[a] ± 18.47	H= 62.591*	<0.001*
Median	120.0	120.0	120.0	120.0	130.0	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	50.0 – 140.0	50.0 – 140.0	50.0 – 140.0		
Mean ± SD.	78.56[c] ± 11.63	78.56[c] ± 11.63	81.14[b] ± 11.71	81.14[b] ± 11.71	83.38[a] ± 11.66	83.38[a] ± 11.66	H= 59.736*	<0.001*
Median	80.0	80.0	80.0	80.0	80.0	80.0		
DM								

	BMI (kg/m²)	**BMI (kg/m²)**	**BMI (kg/m²)**	**BMI (kg/m²)**	**BMI (kg/m²)**	**BMI (kg/m²)**	**Test of sig.**	**p**
Normal	435[a]	90.2	512[a]	87.2	714[b]	80.2	χ^2= 40.488*	<0.001*
New DM	21[a]	4.4	19[a]	3.2	31[a]	3.5		
Controlled DM	12[a]	2.5	25[a]	4.3	62[b]	7.0		
Un controlled 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		
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		

a,b,c : Means with **Common letters** are not significant (i.e. Means with **Different letters** are significant)

χ^2: **Chi square test**

H: H for **Kruskal Wallis test,** Pairwise comparison bet. each 2 groups was done using **Post Hoc Test (Dunn's for multiple comparisons test)**

p: p value for comparing between the **three categories**

*: Statistically significant at p [?] 0.05

Table (3) Relation between age and different parameters in positive H C V (n=1959)

Age (years)

Age (years)

Age (years)

Age (years)

Test of

sig.

p

<40 (n=283)

<40 (n=283)

[?]40 (n=1676)

[?]40 (n=1676)

No.

%

No.

%

Sex

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

χ^2=17.756*

<0.001*

Overweight

96

33.9

491

29.3

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

19.0 – 39.0

40.0 – 94.0

40.0 – 94.0

U= 194612.0*

<0.001*

Mean ± SD.

31.50 ± 5.63

31.50 ± 5.63

57.98 ± 10.04

57.98 ± 10.04

Median

33.0

33.0

58.0

58.0

DM

Normal

273

96.5

1388

82.8

χ^2= 35.913*

<0.001*

New DM

2

0.7

69

4.1

Controlled DM

6

2.1

93

5.5

Un controlled 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

HTN

Normal

277

97.9

1350

80.5

χ^2= 51.667*

<0.001*

Hyper

6

2.1

326

19.5

χ^2: **Chi square test U: Mann Whitney test**

P: p value for comparing between the **two categories**

*: Statistically significant at p [?] 0.05

Table (4) Relation between HTN and different parameters in positive H C V (n=1959)

HTN

HTN

HTN

HTN

Test of

sig.

P

Normal

(n=1627)

Normal

(n=1627)

Hyper

(n=332)

Hyper

(n=332)

No.

%

No.

%

Sex

Male

714

43.9

89

26.8

χ^2= 33.245*

<0.001*

Female

913

56.1

243

73.2

Age (years)

<40

277

17.0

6

1.8

χ^2= 51.667*

<0.001*

[?]40

1350

83.0

326

98.2

Min. – Max.

19.0 – 93.0

19.0 – 93.0

26.0 – 94.0

26.0 – 94.0

U = 153379.50

<0.001*

Mean ± SD.

52.50 ± 13.27

52.50 ± 13.27

62.26 ± 10.28

62.26 ± 10.28

Median

53.0

53.0

63.0

63.0

BMI (kg/m^2)

18.5 – 24.9 (Normal)

444

27.3

38

11.4

χ^2= 69.199*

<0.001*

25 – 29.9 (Overweight)

510

31.3

77

23.2

[?]30 (Obese)

673

41.4

217

65.4

<30

954

58.6

115

34.6

χ^2= 64.048*

<0.001*

[?]30

673

41.4

217

65.4

Min. – Max.

16.41 – 64.84

16.41 – 64.84

17.96 – 57.16

17.96 – 57.16

U = 183448.50*

<0.001*

Mean ± SD.

29.40 ± 6.38

29.40 ± 6.38

33.22 ± 7.16

33.22 ± 7.16

Median

28.39

28.39

32.89

32.89

DM

Normal

1462

89.9

199

59.9

χ^2= 325.072*

<0.001*

New DM

69

4.2

2

.6

Controlled DM

30

1.8

69

20.8

Un controlled DM

66

4.1

62

18.7

χ^2: **Chi square test U: Mann Whitney test**

P: p value for comparing between the **two categories**

*: Statistically significant at p [?] 0.05

Table (5) Univariate and multivariate analysis affecting different parameters in positive HCV (n=1959)

	Univariate	**Univariate**	**#Multivariate**	**#Multivariate**
	P	**OR (95%C.I)**	**p**	**OR (95%C.I)**
Diabetes affecting studied parameters				
Age [?]40 (years)	<0.001*	5.538 (3.141 – 9.765)	0.001*	3.073 (1.584 – 5.
BMI [?]30 (kg/m^2)	<0.001*	1.983 (1.553 – 2.532)	0.022*	1.369 (1.046 – 1.
Systolic ([?]130)	<0.001*	3.342 (2.588 – 4.315)	<0.001*	2.116 (1.505 – 2.
Diastolic ([?]80)	<0.001*	1.845 (1.364 – 2.497)	0.204	0.778 (0.528 – 1.
HTN	<0.001*	5.922 (4.511 – 7.775)	<0.001*	3.910 (2.909 – 5.
BMI [?]30 affecting studied parameters				
Sex	<0.001*	5.058 (4.135 – 6.188)	<0.001*	5.158 (4.190 – 6.
Age [?]40 (years)	<0.001*	1.722 (1.323 – 2.241)	0.009*	1.480 (1.103 – 1.
Systolic ([?]130)	<0.001*	1.803 (1.505 – 2.160)	0.067	1.250 (0.985 – 1.
Diastolic ([?]80)	<0.001*	1.606 (1.311 – 1.966)	0.006*	1.419 (1.106 – 1.
DM	<0.001*	1.913 (1.489 – 2.458)	0.014*	1.436 (1.076 – 1.
HTN	<0.001*	2.675 (2.090 – 3.423)	0.001*	1.627 (1.218 – 2.
HTN affecting studied parameters				
Sex	<0.001*	2.135 (1.643 – 2.774)	<0.001*	2.252 (1.686 – 3.
Age [?]40 (years)	<0.001*	11.148 (4.921 – 25.256)	<0.001*	4.640 (1.985 – 10
Systolic ([?]130)	<0.001*	8.096 (6.014 – 10.900)	<0.001*	5.022 (3.529 – 7.
Diastolic ([?]80)	<0.001*	4.342 (2.972 – 6.344)	0.096	1.479 (0.932 – 2.
DM	<0.001*	5.922 (4.511 – 7.775)	<0.001*	4.183 (3.109 – 5.

OR: Odd's ratio, C.I: Confidence interval,

#: All variables with p<0.05 was included in the multivariate

*: Statistically significant at p [?] 0.05

Discussion:

Within 1959 patients, this study illuminates the effect of cofounding factors such as HTN, DM, BMI, age and gender in patients having HCV virus infection. Illustrating each of these points depends on a multivariate analysis for diverse parameters and patients risk factors in positive HCV patients. After analyzing the results of the study, infected female patients were found to be more with (1156) patients with 59 %, and male patients where 803 patients with 41 %. Infected patients aged [?] 40 year old were 85.6 % , Obese

patients with BMI [?] 30 (Kg/ m2) were 45.4 % and patients with uncontrolled blood pressure with systolic blood pressure [?] 130 mm.Hg were (43.7 %) and diastolic blood pressure [?] 80 mm.Hg were 72.1%.

In this study we found that in all patients with chronic HCV that the age [?] 40 , BMI [?] 30 (Kg/ m2) and high systolic blood pressure with esteem of [?] 130 mm.Hg , are all independent factors for DM2. These findings suggest that ageing , being corpulent and having a high uncontrolled blood pressure all together with positive HCV infection increases the rates of glucose abnormalities including anomalies in carbohydrate metabolism, insulin resistance, metabolic clutters which may progress into DM2 [14] .

Several studies had mentioned some explanations for this hypothesis which is increasing risk of getting DM in HCV infected patients . In an important study by Abdelaziz, S.B., et al, suggesting that diabetic patients might get infected due to contaminated injections or nosocomial transmission, but this hypothesis was reduced due to the widespread use of universal precautions in hospitals. Other possible mechanisms include that the progressive increase of liver fibrosis and cirrhosis as common complications of being HCV positive patient [14] are inducing glucose metabolism impairment or reduction in glucose uptake by the cells [1] . Cirrhosis itself is considered diabetogenic . On the other hand, diabetes can worsen hepatitis C outcomes, including increasing the risk for cirrhosis and hepatocellular carcinoma (HCC) [16] [17] . .

Also, another study has suggested that eradication of HCV patients with direct-acting antiviral (DAA) therapy leads to improved glycemic control in patients with T2DM , decrease level of HbA1c and decrease the proportion of patients taking insulin [18] .

For other factors linking being diabetic and HCV positive patient, as mentioned before females have higher rate than men in the current study and another study [1] . Unlike other studies which found that Hepatitis C is more common among men than women , and male gender is also associated with more hepatitis C disease progression to fibrosis and cirrhosis [16] .

Occurrence and recurrence of HCC are high among patients with chronic HCV infection, obesity, and heavy alcohol intake. Also, nonalcoholic fatty liver disease (NAFLD) due to obesity by itself can increase the inflammation of liver or cause other obesity-related diseases [19]. [20]. Also in this current study , one of the interesting finding was the impact of BMI , as the multivariate analysis in the study revealed that having BMI [?] 30 (Kg /m2) affects different parameters in HCV positive patients. The study noticed that the incidence of getting HCV infection is highly increased in those obese, aged [?] 40 years, diabetic [?] 200 mg/dL and with uncontrolled blood pressure (diastolic blood pressure [?] 80 mm.Hg) .

In Ali-Eldin, Z.A., et al, study showed that free fatty acid and cytokine secretion induced by adipose tissue dysfunction may contribute in both liver steatosis and induction of inflammation and as a result fibrosis level and the degree of hepatic affection in chronic HCV patients. Furthermore, changes in glucose metabolism which results into insulin resistance as mentioned before , all are associated with more liver disease , so changes in the hosts lipid metabolism due to chronic HCV increase viral replication, which can lead to steatosis and may affect the efficacy of interferon-based therapy. This represents a novel target for therapeutic intervention in HCV eradication [21] .

Another vital factor in the multivariate analysis is that cardiovascular diseases appear to be increased with higher rate of morbidity and mortality especially hypertensive patients with blood pressure [?] 130 mm.Hg (with systolic blood pressure [?] 130 mm.Hg and diastolic blood pressure [?] 80 mm.Hg) , and also BMI [?] 30 (kg/m2) [22] . Unlike other studies which depends only on hypertension and diabetes and showed two-fold higher risk of subclinical carotid plaques among HCV-infected individuals compared to uninfected controls and increase in the rate of peripheral arterial diseases as well. This maybe due to the severity of the liver damage or even due to direct viral activity [23] .

In recent study untreated HCV infected persons have twice risk of CVD (Cardiovascular diseases) as: (coronary artery disease events, acute myocardial infarction, congestive heart failure, unstable angina, and revascularization procedures, stroke and peripheral vascular disease) than those who initiated treatment [24]. As a result, significant benefit of HCV treatment on the incidence and risk of possible CVD events in the

future [24]. Other studies have mentioned that co-infection with both HCV/HIV viruses are associated with more risk to CVD [25] [26], so reduction in survival is obvious in HIV/HCV- coinfected patients than HIV-monoinfected patients and HIV-coinfected patients without cirrhosis [27] . Concerning another study, persistent HCV replication leads to a state of systemic inflammation and immune activation that leads to endothelial dysfunction, atherosclerosis and increased CVD risk [15] .

Limitations:

First, the sample size was relatively small which may have influenced the statistical outcome. Second, individual variations between the patients as, marriage, rural residence, injections for bilharzias, blood transfusion, acupuncture and tattooing were not taken in consideration. Third, Lack of data on the severity of liver fibrosis, can affect the judgement on some cases. Fourth, the dependence on 'self-reporting' for the cardiovascular diseases may limit the number of these reports , and also lack of laboratory data of lipid and lipoprotein profile and the level of liver enzymes and not accounting for their potential elevation may confound the association of diabetes and of the cardiovascular events all together with HCV infected patients.

Conclusion;

On the light of the results of the present study, it was found that HCV infection triggers metabolic disorders to happen, abnormalities of carbohydrate metabolism, including hyperinsulinemia, insulin resistance and diabetes especially type 2 which arises from steatosis and inflammatory processes. Also it was found that diabetes worsens hepatitis C outcomes 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 on patients. Uncontrolled blood pressure may increase the risk for (CVD), increase in the rate of peripheral arterial diseases, carotid plaques, endothelial dysfunction and atherosclerosis so controlling blood pressure of the patient would be helpful reducing the incidence of serious CVD. Obese patients with BMI [?] 30 (kg/m2) and the free fatty acid secretions may increase the inflammation, changing of lipid-cholesterol biosynthesis that causes fatty liver occurrence, hypercholesterolemia and as a result fibrosis. Controlling patient weight helps preventing complications associated with HCV infection as fibrosis and hepatocellular carcinoma.

Data Availability :

All data generated or analyzed during this study is included in this published article will be available upon request.

Financial support

No financial support was provided

Ethics declarations

Conflict of interest

All authors declare that they have no conflict of interest.

Ethical Approval

The authors declare that all procedures contributing to this work comply with the ethical standards of Scientific Ethics Committee Board at the University of Pharmacy Damnhour university. This study was approved by the University hospital and patients signed informed consent forms before starting the study.

List of abbreviations:

CVD: Cardiovascular Disease

HCV: Hepatitis C virus

BMI: Body mass index

DM2: Diabetes Mellitus type 2

T2DM: Type 2 Diabetes Mellitus

HbA1c: Glycated Hemoglobin

HCC: Hepatocellular Carcinoma

NAFLD: Non-alcoholic fatty liver disease

PLC: Primary Liver Cancer

HIV: human Immunodeficiency Viruses

ALT: Alanine Aminotransferase

AST Aspartate Aminotransferase

SPSS Statistical package for the social science

BGL Blood glucose level

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