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Original Article

Internal Medicine Section

Visceral Adiposity Index and the Degree of Hepatic Fibrosis and Inflammation in Egyptian Patients with Chronic Hepatitis C

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ABSTRACT

Introduction: Many clinical studies suggest a direct association between hepatic fat content and visceral adiposity and the progression of fibrosis.

Aim: This work aims to clarify the relation between the Visceral Adiposity Index (VAI) and severity of necroinflammatory activity and liver fibrosis in Egyptian patients with chronic Hepatitis C Virus (HCV) infection.

Materials and Methods: A cross-sectional study, over a period of six months, was performed on 50 chronic HCV patients subjected to routine laboratory investigations, abdominal ultrasonography, measurement of Waist Circumference (WC), calculation of Body Mass Index (BMI) and VAI, ultrasound guided liver biopsy and assessment of hepatic fibrosis by METAVIR staging.

Results: A total of 50 HCV positive patients, 29 (58%) males and 21 (42%) females were included in the study. Age ranged from 29-60 years (44.4±8.4). BMI was ranged from 20.3 to 41.4 kg/m^2 (31.7±5.5). VAI for males was 0.4±0.2 and for females was 0.5±0.3. There were significant positive correlations between VAI and BMI, Triglycerides (TG), fibrosis stages, grades of liver inflammation and FIB-4 Fibrosis-4 score. There were significant negative correlations between VAI and high density lipoprotein, platelets and haemoglobin.

Conclusion: There is an association between visceral obesity represented by VAI and the severity of hepatic inflammatory response in chronic hepatitis C patients. Other studies are recommended to measure the clinical implication of visceral obesity on the response to the novel directly acting antivirals.

Keywords: Liver fibrosis, Viral hepatitis, Visceral obesity

INTRODUCTION

Hepatitis C is an infectious disease affecting primarily the liver, caused by the HCV. The infection is often asymptomatic, but chronic infection can lead to scarring of the liver and ultimately to cirrhosis, which is generally apparent after many years [1]. Almost 20% of chronic HCV patients are obese, obesity ends with steatosis and hepatic scarring [2-6].

Clinical studies suggest a direct association between hepatic fat content and visceral adiposity [7]. Imaging modalities as magnetic resonance imaging that estimates abdominal fat in obese and non-obese individuals have found correlations between visceral and liver fat content. Importantly, visceral fat is directly linked to the severity of liver inflammation and fibrosis [8]. Furthermore, hepatic steatosis, which might be associated with the progression of necro-inflammation and fibrosis in chronic HCV infection, can develop secondary to obesity and insulin resistance [9].

HCV infection induces hepatic steatosis through different mechanisms. Activity of Microsomal Triglyceride Transfer Protein (MTP), a luminal protein involved in Very Low Density Lipoprotein (VLDL) assembly and export, reduced via chronic hepatitis C [10,11]. Moreover, increased intracellular lipids due to decrease in VLDL export is related to severity of hepatic steatosis [12].

VAI, a sex-specific index, has been developed based on: WC, BMI, TG and HDL. It was observed that VAI is highly correlated with visceral adiposity measured by magnetic resonance imaging [13].

Several studies worked on the relation between visceral fat and VAI and severity of hepatic necroinflammation and fibrosis in patients with non alcoholic steatohepatitis [14,15], but little data exists about its role in HCV infected patients.

This study aimed to clarify the relation between the VAI and hepatic necroinflammatory activity and liver fibrosis in patients with chronic HCV infection.

MATERIALS AND METHODS

A cross-sectional study was performed on 50 chronic HCV-patients, from January 2016 to June 2016, they were recruited from Ain Shams University outpatient clinics Egypt.

Inclusion criteria: Chronic HCV patients whose age ranged from 17 to 60-year-old and were indicated to have liver biopsy.

Ethical considerations: This study has been performed in accordance with the ethical standards. Faculty of Medicine, Ain Shams University Ethical Committee approval was taken before starting the study. Written informed consent was obtained from all participants before enrolment in the study.

Patients with HBV infection (positive HBsAg), heavy alcohol consumption (80 g/day for five years), previous Interferon (IFN) or ribavirin therapy, autoimmune disease (i.e., autoimmune hepatitis, rheumatoid arthritis and systemic lupus erythematosus), and diabetes mellitus were excluded from the study.

All participants were subjected to: Full history taking, clinical examination, BMI calculation and measurements of WC at the mid-point between the lower margin of the last palpable rib and the top of the iliac crest [16].

Laboratory investigations including complete blood count, liver function tests (transaminases, total bilirubin, albumin), fasting blood sugar, 2-hour postprandial blood sugar, HbA1c, AFP, creatinine, prothrombin time, INR, HBsAg, anti-bilharzial antibody and anti-nuclear antibody.

After 12-hours fasting, a venous sample is withdrawn to determine TG, and HDL- cholesterol levels.

(FIB-4) was calculated for all patients as follow: FIB-4 = [age (years) x AST] /{platelet (109/ l) x √ALT} [17].

Abdominal ultrasound and ultrasound guided liver biopsy: Percutaneous liver biopsy: Ultrasound guided liver biopsy performed using 16-gauge needles. All specimens 2.5 cm in length, of at least 12 portal tracts included and serial sections of formalin-fixed, paraffin-embedded blocks were stained with haematoxylin & eosin. Assessment of hepatic fibrosis using METAVIR staging of liver scarring [18].

Calculation of VAI according to the following formula:

Males: VAI =)WC/39.68+1.88 x BMI(x)TG/1.03(x)1.31/HDL

Females: VAI=) WC/36.58+1.89 x BMI(x)TG/0.81(x)1.52/HDL) [19].

STATISTICAL ANALYSIS

The data were collected, revised, verified then edited on a personal computer. For quantitative parametric data minimum and maximum range was taken, in addition to, mean±SD (standard deviation). For qualitative data, number and percentage were used.

Correlations were done using Pearson correlation for numerical parametric data, and using Spearman rho test for qualitative ordinal data.

The level of significance was taken at p-value < 0.05 is significant, otherwise is non-significant.

RESULTS

This study included 50 HCV positive patients; 29 (58%) males and 21 (42%) females. Their ages ranged from 29-60 years (44.4±8.4). Mean BMI was 31.7±5.5kg/m^2 (20.3–41.4). WC ranged between 65-120 cm (93.0±11.5). VAI for males was 0.4±0.2 and for females was 0.5±0.3.

Baseline characteristics of the cases were described in [Table/Fig-1].

Results of histopathological examination of liver biopsy and FIB-4 are shown in [Table/Fig-2].

There is a highly significant relation between VAI and the degree of liver fibrosis (p<0.001). Also, there is a highly significant relation between VAI and the grade of necroinflammation (p<0.001) [Table/Fig-3].

Significant positive correlations were present between VAI and AST, fibrosis stages, grades of liver inflammation and FIB-4. There were significant negative correlations between VAI, and platelets and haemoglobin. There is a highly significant relation between VAI and the degree of liver fibrosis (p<0.001). Also, there is a highly significant relation between VAI and the grade of necroinflammation (p<0.001). There was a significant positive correlation between fibrosis stages; and age, BMI, TG, AST, necroinflammatory grades. A positive correlation was found between fibrosis and WC although, it was statistically non-significant. There were significant negative correlations between fibrosis and HDL, platelets and haemoglobin [Table/Fig-4].

DISCUSSION

In chronic HCV infection, assessment of liver fibrosis is an important part in patient care and key for decision making. Liver fibrosis stage is also an important prognostic factor in many liver diseases including chronic HCV infection [20].

In addition, the severity of liver fibrosis affect the selection of antiviral therapy and the need for further follow-up, such as screening for Hepatocellular Carcinoma (HCC) and oesophageal varices [21].

The present study tried to find a relation between VAI and degree of hepatic affection in patients with chronic HCV infection.

The results of the present study showed that there is no significant correlation between histopathological degree of fibrosis and WC. On the contrary, Bailony MR [22] documented that among patients

Variable	N	%
Sex Male Female	 29 21	 58.0 42.0
Diabetes mellitus	8	16.0
	Mean±SD	Range
Anthropometric measures		
Age (years)	44.4±8.4	29.0–60.0
BMI (kg/m^2)	31.7±5.5	20.3–41.4
WC (cm)	93.0±11.5	65–120
Laboratory finding		
TG (mg/dL)	129.8±35.7	66.0–189.0
HDL (mg/dL)	45.8±13.0	24.0–68.0
AST (IU/L)	40.8±13.5	17.0–108.0
ALT (IU/L)	38.9±14.5	23.0–109.0
PLT (x103/mL)	155.0±62.8	63.0–281.0
WBC (x103/mL)	6.0±1.3	3.2–9.0
Hb (gm/dL)	13.5±1.6	10.5–17.0
VAI	0.45±0.26	0.12–1.1

[Table/Fig-1]: Descriptive data of the studied cases.

Variable	Grades	N	%
Fibrosis stages	F1	12	24.0
	F2	9	18.0
	F3	8	16.0
	F4	21	42.0
Necroinflammatory grades	A1	19	37.5
	A2	23	45.8
	A3	8	16.7
Steatosis	Absent	44	87.5
	Present	6	12.5
FIB-4	Mean ± SD	2.3 ± 1.3	
	Range	0.7–4.8	

[Table/Fig-2]: Fibrosis stages, necroinflammatory grades, steatosis and FIB-4 for the studied patients.

with HCV alone or HIV/HCV coinfection, an association was noted between WC and liver stiffness, with 18.7% increased stiffness for every 10 cm increase in circumference (P=0.001).

There was highly significant positive correlation between VAI and grades of liver inflammation (p<0.001). This agrees with Petta S et al., who studied VAI and its association with histological findings in patients with chronic hepatitis C due to genotype 1 and found that higher VAI score were independently associated with moderate to severe necroinflammatory activity (OR 1.618, 95% CI 1.001-2.617, p=0.04) [19].

On the contrary, Eguchi Y et al., who analysed 87 HCV-infected patients with mild fibrosis (stage 1 or 2) in comparison with 125 sex and age matched patients with Non-Alcoholic Fatty Liver Disease (NAFLD), concluded that visceral obesity in HCV-infected patients were not correlated to HCV viral loads, genotypes or distributions of histological activity and steatosis [23]. This difference might be attributed to the lower fibrosis stage in their study in comparison to the present study.

The present study reported a positive correlation between VAI and degree of fibrosis (p<0.001). This was against Petta S et al., who found no association between severe fibrosis and VAI score [19]. This difference in results may be due the different genotypes of HCV in both studies.

According to Ticehurst JR et al., high VAI was associated with moderate to severe necroinflammatory activity in chronic HCV genotype 1 infection; a higher VAI also has a direct correlation with viral load [24].

Variable	r	p
Age	0.270#	0.058
BMI	0.383#	0.006*
WC	0.003#	0.982
TG	0.837#	<0.001*
HDL	-0.846#	<0.001*
AST	0.328#	0.020*
ALT	-0.154#	0.287
Platelets	-0.763#	<0.001*
WBC	-0.084#	0.562
Haemoglobin	-0.479#	<0.001*
Fibrosis stages	0.950^	<0.001*
Grades of necroinflammation	0.753^	<0.001*
FIB-4	0.878#	<0.001*

[Table/Fig-3]: Correlation between VAI and other variables.
#Pearson correlation, ^Spearman correlation, *Significant

	Liver Fibrosis		FIB-4	
Variable	r	p	r	p
Age	0.356	0.011	0.395#	0.004*
BMI	0.341	0.015	0.359#	0.011*
WC	0.181	0.208	0.091#	0.529
TG	0.866	0.001	0.807#	<0.001
HDL	-0.891	0.001	-0.813#	<0.001
AST	0.473	0.001	0.446#	<0.001
ALT	0.014	0.922	-0.051#	0.727
Platelets	-0.818	0.001	-0.862#	<0.001
WBC	0.022	0.877	-0.176#	0.222
Haemoglobin	-0.396	0.004	-0.328#	0.020
Grade	0.840	0.001	0.326^	0.120

[Table/Fig-4]: Correlation between liver fibrosis stages, FIB-4 and other studied variables.
#Pearson correlation, ^Spearman correlation,

Free fatty acid and proinflammatory cytokine secretion induced by adipose tissue dysfunction (expressed by the VAI) may contribute in both liver steatosis and induction of inflammation.

There was a highly significant positive correlations between fibrosis and grade of liver inflammation (p<0.001). This agreed with previous study which found that greater levels of liver inflammation were associated with severe fibrosis [19].

A significant negative correlation was found between VAI and platelets, similar results were reported by Petta S et al., [19].

Our results proved that there is a definite relation between chronic HCV infection and the visceral adiposity, and this may reflect the inter-relationship between VAI and the degree of hepatic affection in chronic HCV patients.

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. Furthermore, changes in glucose metabolism induced by chronic hepatitis C result in insulin resistance, which promotes hepatic steatosis and more advanced liver disease. If lipid metabolism is involved in HCV infectivity and replication, this represents a novel target for therapeutic intervention in HCV eradication [25].

All the studies mentioned the relation between obesity, VAI; and the degree of fibrosis and necroinflammatory activity are performed on HCV genotypes other than genotype 4 which is more prevalent in Egypt, this study tried to find out such relation.

LIMITATION

Relatively small number of patients as indications of liver biopsy is limited and replaced in many clinical situations with non invasive methods.

CONCLUSION

There is an association between visceral obesity represented by VAI and the severity of hepatic inflammatory response in chronic hepatitis C patients. Other studies are recommended to measure the clinical implication of visceral obesity on the response to the novel directly acting antivirals.

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