Metabolic Factors Associated with Hepatic Steatosis and Fibrosis in Patients with Chronic Hepatitis C

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Abstract

Objective: Hepatic steatosis is a common histological feature in chronic hepatitis C (CHC), but its pathogenic mechanisms are not completely understood. We aimed to evaluate the metabolic factors associated with hepatic steatosis and fibrosis in CHC patients, and the relation between metabolic syndrome (MS) and CHC.

Patients and Methods: This study included 71 patients with chronic HCV infection who underwent clinical, BMI, biochemical (assessment of insulin resistance, serum adiponectin, TNF-α, cholesterol and triglycerides), virological and histological assessments.

Results: Of 71 patients with CHC. Significant steatosis (>33%) was detected in 54% of the patients, while 21.12% of the patients had stage 3/4 fibrosis. Higher degree of steatosis was significantly associated with BMI, serum insulin, HOMA index and TNF-α ($P < 0.0001$, $P < 0.0006$, $P < 0.0001$, and $P < 0.01$ respectively). Higher stages of fibrosis were significantly associated with BMI and serum triglycerides ($P < 0.04$; $P < 0.02$ respectively). Multivariate analysis of the metabolic factors shows that HOMA index ($P < 0.001$) and TNF-α ($P < 0.03$) are the factors mostly predicting higher degree of steatosis. While, BMI index ($P < 0.01$) and serum triglycerides ($P < 0.03$) are the factors mostly predicting higher stage of fibrosis. We also found that CHC is closely related to MS, and we recognized that age ($P<0.011$), BMI ($p<0.0001$), serum adiponectin (0.0001), TNF-α ($p<0.0001$) and steatosis degree ($p<0.04$) are significantly associated with MS in these patients.

Conclusions: In patients with CHC, higher BMI, HOMA-IR, lower serum adiponectin and higher serum TNF-α and triglycerides were associated with HCV hepatic steatosis and metabolic syndrome, while higher BMI and serum triglycerides were associated with more advanced fibrosis.

Keywords: CHC, BMI, adiponectin, TNF-α: tumor necrotic factor-α, HOMA: homeostasis model of assessment.

Introduction:

Hepatitis C virus (HCV) infection is an important public health problem because approximately 170 million people are infected worldwide. Chronic liver disease results from persistent infection in the majority of patients infected with the virus [(1)]. The Egyptian Demographic Health Survey (EDHS), a cross sectional survey including hepatitis C virus (HCV) biomarkers, was conducted in 2008 on a large nationally representative sample [(2)]. It estimated HCV prevalence among the 15–59 years age group to be 14.7%. Accordingly, Egypt has the highest HCV prevalence in the world [(3)]. HCV steatosis was recently identified as a risk factor for progression to extensive fibrosis [(4)]. Liver steatosis is a common finding in patients infected with hepatitis C virus (HCV) [(5)]. Chronic HCV infection is closely related to the metabolic syndrome (MS). Accordingly, CHC should be classified into CHC with and CHC without MS. Insulin resistance (IR) is the main feature of the MS. In CHC, there is a close association between IR, hepatic steatosis [(6)], progression of fibrosis [(7)].

The adipocytokine profile seems to play a distinct role, together with IR, in the pathogenesis of CHC [(8)]. Adiponectin modulates hepatic fat content and has an anti-steatotic effect on the liver [(9)]. Adiponectin is also a hepatic insulin sensitizer and has the opposite effect in comparison with tumor necrotic factor (TNF-α) on lipid metabolism, insulin sensitivity and inflammation [(10)]. In CHC, adiponectin levels are also associated with the degree of steatosis and insulin resistance [(11)]. Abnormalities of lipid metabolism such as the increase of serum triglyceride, cholesterol and LDL-cholesterol level and decrease in HDL-cholesterol may be the contributing factors in the development of NASH [(12).]

Aim of the work:

To assess which factors associated with hepatic steatosis and fibrosis in patients infected with CHC, and to assess the impact of insulin resistance (as measured by HOMA-IR score) and serum adipocytokines levels on hepatic steatosis and fibrosis relative to other factors. Finally, to evaluate the relationship between CHC and metabolic syndrome.

Patients and Methods:

The present study included 71 patients (22 females and 49 males) with chronic hepatitis C (HCV). Their ages ranged between (21-57 years). All patients were referred to the Department of Tropical Medicine and Gastroenterology, Sohag University Hospital and to Sohag Specialized Liver Institute (in the period from August 2011 to Septemper 2013) for doing liver biopsies and the complementary laboratory tests before starting treatment with pegylated interferon and ribavirin therapy at Sohag Specialized Liver Institute. Before inclusion in the study, all participants gave an informed consent and the study protocol was approved by the Local Ethics Committee.

In addition, 12 adult age and sex matched healthy individuals were also included to serve as a control group.

Patients were diagnosed as chronic hepatitis C based on clinical

data and positive anti-HCV by ELISA test and HCV RNA by PCR for more than 6 months.

Exclusion criteria:

Patients were excluded if they have any of the following:

- Hepatitis B virus co-infection,
- Autoimmune disease.
- Alcohol consumption.
- Decompensated liver disease.
- Pregnancy or breast feeding.
- Patient with other medical disease as renal or ischaemic heart disease, significant retinal abnormality, uncontrolled neuropsychiatric disease, immunologically mediated disease, organ transplantation

Methods:

The following were done to all patients:

- Complete history taking and full clinical examination.

Body mass index was calculated from patients' weight: patients' weight (Kg)/ patients' height (meter) ^{2}.

- **Investigations:**

1) Laboratory:

a) Liver function tests: serum albumin, ALT, AST, total bilirubin, direct & indirect bilirubin, prothrombin time and concentration by standard methods.

b) Fasting serum glucose, creatinine, complete blood

c) Polymerase chain reaction (PCR).

d) Serum cholesterol and triglycerides.

e) Measurement of serum adiponectin and serum TNF-α.

f) Serum insulin to calculate HOMA index

2) Abdominal ultrasonography.

3) Histopathological assessment:

Seventy one liver biopsies were included in the study and submitted to histopathological examination. Hematoxylin and eosin (H&E) stained sections were done to assess both the grade and the stage of chronic viral hepatitis, in addition to the degree of steatosis. Metavir grading and staging systems were used

Statistical analysis:

Data were computed and analyzed using STATA intercooled version 9.2. Quantitative data was analyzed using ANOVA test and Post Hoc Bonferroni test for comparison of the means of three groups. When the data were not normally distributed Kruskal –Wallis rank test and Mann-Whitney test was used. Qualitative data were compared using Chi square test. P value was considered significant if it was less than 0.05. Both univariate and multivariate analyses were used to determine risk factors (predictors) of significant steatosis (moderate and severe), and the same was performed to determine the risk factors (predictors) of advanced fibrosis (stage 3 and 4).

Results

This study was conducted on 71 patients with chronic hepatitis C who fulfilled the study's inclusion criteria. The patients were predominantly males (49 males and 22 females), with ages ranging from 20 - 57 years and a mean age of 41.86 ±9.70. Besides, 12 persons served as controls (7 males and 5 females), with ages ranging from 22-50 years and a mean age of 41.75 ± 7.66. According to the histopathology reports, the studied patients were classified according to the degree of steatosis into 2 groups: **Steatosis group 1:** includes 33 patients (46.5%) with chronic hepatitis C and steatosis < 33%. **Steatosis group 2**: includes a total of 38 patients (53.5%) with chronic hepatitis C and steatosis > 33%.

The same patients were also categorized according to the fibrosis score into 3 groups: **Fibrosis group 1**: includes 40 patients (56.3%) with fibrosis score F 0/1. **Fibrosis group 2**: includes 16 patients (22.5%) with fibrosis score F2. **Fibrosis group 3:** includes 15 patients (21.1%) with fibrosis score F 3/4.

Table (1): Comparison between each steatosis group and controls

Characteristic	Steatosis group1 N=33	Steatosis group 2 N=38	Controls N=12	Steatosis group 1 vs group 2	Steatosis group 1 vs controls	Steatosis group 2 vs controls
Age						
Mean (SD)	39.88 (10.35)	43.62 (8.85)	41.75 (7.66)	0.11	0.52	0.09
Median (range)	42 (20-56)	44 (22-57)	38 (22-50)			
Gender						
Males	25 (75.76%)	24 (64.86%)	7 (58.3%)	0.32	0.09	0.36
Females	8 (24.24%)	13 (35.14%)	5 (41.7%)			
Body mass index (BMI)						
Mean (SD)	25.60 (3.42)	29.2 (3.57)	24.33 (1.82)	**0.0001**	0.23	**<0.0001**
Median (range)	25 (18-31)	29 (23-35)	24.5 (20-26)			
ALT (IU/L)						
Mean (SD)	62.45 (41.49)	72.89 (79.01)	32.58 (5.14)	0.83	**0.001**	**0.0002**
Median (range)	51 (13-202)	55 (26-489)	32.5 (25-41)			
AST (IU/L)						
Mean (SD)	47.45 (22.03)	63.89 (67.06)	29.17 (5.89)	0.24	**0.004**	**0.0001**
Median (range)	45 (12-105)	50 (19-429)	27.5 (22-40)			
HOMA						
Mean (SD)	1.67 (0.66)	3.44 (0.77)	1.42 (0.40)	**<0.0001**	0.32	**<0.0001**
Median (range)	1.5 (0.8-3.5)	3.5 (1.7-4.6)	1.35 (0.9-2.1)			
Adiponectin (ng/ml)						
Mean (SD)	26.45 (4.50)	20.49 (5.01)	28.45 (4.03)	**<0.0001**	0.19	**<0.0001**
Median (range)	26.1 (16.8-40.8)	20.4 (3.7-29.3)	27.05 (23.2-35.4)			
TNF-α (pg/ml)						
Mean (SD)	100.29 (41.25)	128.01 (47.21)	49.47 (9.58)	**0.01**	**0.0001**	**<0.0001**
Median (range)	101.8 (30.7-231.5)	127.5 (38.5-221)	49.6 (37-63.1)			
Triglyceride (mg/dl)						
Mean (SD)	115.06 (30.82)	139.86 (34.72)	96.25 (11.69)	**0.003**	**0.046**	**0.0001**
Median (range)	101 (79-198)	141 (79-194)	97.5 (77-114)			
Cholesterol (mg/ dl)						
Mean (SD)	142.55 (29.85)	153.68 (39.78)	130 (21.85)	0.19	0.19	0.06
Median (range)	132 (104-205)	160 (97-228)	129 (98-165)			
Viral load						
Mean (SD)	760591.5 (1205421)	523987.7 (992435.9)		0.71		
Median (range)	230000 (212-6104311)	184347 (8500-5447004)				

When the two groups were compared regarding their laboratory data, we found that both BMI, serum insulin and HOMA index were significantly higher in group 2 than group 1 (P <0.0001, P <0.0006 and P< 0.0001, respectively). Serum adiponectin was significantly higher in group 1 (P <0.0001), while serum TNF-α was higher in group 2 (P <0.01). Serum lipogram shows significantly higher triglycerides in group 2

(P <0.003). While no significant difference was found between the two groups as regards age, gender and other laboratory variables **(Table 1)**. No significant difference was found in HCV viral load among the two groups of steatosis. Patients in group 1 have significantly higher serum ALT and AST levels (< 0.001, < 0.004 respectively), TNF-α (P <0.0001), serum triglycerides (< 0.046), compared to the controls. While patients in group 2 have higher ALT and AST levels (P <0.0002, <0.0001 respectively), BMI (P < 0.0001), HOMA index, serum TNF-α, serum triglycerides (P < 0.0001 for each), higher serum insulin (P <0.02) compared to the controls. On the other hand, serum adiponectin was significantly lower in group 2 than the controls (P < 0.0001).

Table (2): Laboratory and clinical results of studied groups within each stage of brosis

Characteristic	Stage 0/1 N=40	Stage 2 N=15	Stage 3/4 N=15	Comparosin between each stage of fibrosis	stage 1 vs stage 2	stage 1 vs stage 3/4	stage 2 vs stage 3/4
AST (IU/L)							
Mean (SD)	46.73 (18.82)	49.4 (19.56)	88 (101.25)	0.19	0.56	0.07	0.31
Median (range)	44.5 (19-93)	47 (26-105)	54 (12-429)				
ALT (IU/L)							
Mean (SD)	56.05 (31.27)	66.4 (42.39)	101.33 (118.33)	0.27	0.26	0.16	0.68
Median (range)	49.5 (13-181)	59 (26-202)	61 (20-489)				
Adiponectin (ng/dl) **Mean (SD)** **Median (range)**	23.19 (4.45) 22.6 (9.5-33.8)	23.25 (5.52) 25 (5.7-27.8)	24.19 (5.38) 23.4 (16.3-38.8)	0.79	1.00	1.00	1.00
TNF-α (pg/dl) **Mean (SD)** **Median (range)**	106.21 (44.09) 103.7 (30.7-231.5)	117.89 (54.85) 100.6 (38.5-213.6)	135.27 (38.51) 137.5 (79.3-221.3)	0.11	1.00	0.12	0.90
Triglyceride (mg/dl) **Mean (SD)** **Median (range)**	119.08 (32.14) 108.5 (79-191)	133.87 (35.25) 131 (92-194)	146.73 (35.74) 144 (79-198)	**0.02**	**0.45**	**0.03**	0.89
Cholesterol (mg/dl)							
Mean (SD)	147.38	163.67 (40.21)	136 (29.89)	0.09	0.39	0.86	0.10
Median (range)	(34.59) 144 (97-219)	164 (110-228)	121 (109-210)				
Viral load (copies/ml)	679725.9	478240.5	674961.4	0.44	0.56	0.30	0.27
Mean (SD)	(1325751)	(724249.2)	(684944.6)				
Median (range)	186494.5 (212-6104311)	129000 (23000-2233381)	566214 (1225-2255361)				
Body mass index (BMI) **Mean (SD)** **Median (range)**	25.02 (3.45) 24 (18-31)	25.69 (3.20) 26 (19-31)	29.07 (3.93) 26 (20-31)	**0.04**	1.00	**0.01**	**0.01**

Table2 shows the clinical characteristics of studied population within each stage of fibrosis. We did not find any significant difference between the 3 groups of the studied population as regards serum adiponectin, TNF-α and HOMA index. While a significant difference was found in BMI, being highest in stage 3/4 fibrosis (P< 0.04), serum triglycerides, being highest in group 3 (P <0.02). As with steatosis, we found no difference among the three groups as regards ALT, AST.

Table (3): Characteristics of CHC patients according to the presence or absence of metabolic syndrome

Variables	Metabolic syndrome		
	absent	present	P
Number	46	25	
Age	46.08 ± 4.32	48.68± 3.84	**0.011**
Gender			
Male: (n, %)	32 (65%)	17 (35%)	0.89
Female: (n, %)	14 (64%)	8 (36%)	
BMI	24.24 ±1.74	28.8 ±3.5	**<0.0001**
Blood pressure >130/85 mmHg (n,%)	22 (47.8)	21 (84)	**<0.003**
ALT (IU/L)	57.56 ±44.23	74.41 ± 76.22	0.21
AST (IU/L)	46.33 ±26.01	62.45 ± 64.38	0.14
Total serum cholesterol (mg/dl)	132 ± 26.18	157 ±32.33	**0.0007**
HDL-cholersterol (mg/dl)			
< 40 (M)	41.2 ± 2.1	38.5 ±2.45	**0.002**
< 50 (F)	52.34 ± 6.23	50.58 ±5.66	0.2326
Serum triglycerides (<150 mg /dl)	118.25 ± 78	178.85 ±45	**0.003**
Fasting glucose (mg/dl)	99.04 ±2.41	116.23 ±3.65	**<0.0001**
Fasting insulin (µU/ml)	1.78 ±1.4	3.18 ± 2.2	**0.002**
HOMA-IR	1.4 ± 0.54	3.66 ± 0.78	**<0.0001**
Adiponectin (ng/dl)	27.33 ± 4.7	21.02 ± 3.7	**<0.0001**
TNF-α (pg/dl)	98.54 ±31.29	130.05 ± 39.65	**<0.0001**
Steatosis degree: (n ,%)			
Group 1:	26/33 (78.9%)	7/33 (21.2%)	**0.04**
Group 2:	20/38 (52.63%)	18/38 (47.4)	
Fibrosis: (n, %)			
F 0/1: (n= 40)	30 (75%)	10 (25%)	
F 2: (n= 16)	10 (63%)	6 (37%)	0.64
F 3/4: (n= 15)	11 (73%)	4 (27%)	

To assess whether hepatic steatosis in the current series is related to the presence of metabolic syndrome, patients were re-categorized into a group without MS (n=46) and a group with MS (n=25). We found 12 variables significantly related to the MS namely: age, BMI, elevated blood pressure more than 130/80 mmHg, total serum cholesterol, HDL- cholesterol in males, serum triglycerides, fasting blood glucose, fasting serum insulin, HOMA-IR, serum adiponectin, serum TNF-α and steatosis degree **(Table 3)**.

Table (4): Multivariate analysis for the factors predicting higher stage of steatosis

Variables	Odds ratio (95% Confidence Interval)	P value
HOMA index	0.004 (0.00-0.13)	0.001
TNF-α	0.97 (0.94-0.0.99)	0.03

Table (5): Multivariate analysis for the factors predicting higher stage of fibrosis

Variables	Odds ratio (95% Confidence Interval)	P value
HOMA index	0.004 (0.00-0.13)	0.001
TNF-α	0.97 (0.94-0.0.99)	0.03

Table 4 shows multivariate analysis of the factors mostly predicting higher degree of steatosis, and from this we noticed that HOMA index (P <0.001) and TNF-α (P <0.03) are the factors mostly predicting higher degree of steatosis. **Table 5** shows multivariate analysis of the factors mostly predicting higher degree of fibrosis, and from this we noticed that BMI index (P <0.01) and serum triglycerides (P <0.03) are the factors mostly predicting higher stage of fibrosis.

Discussion

Chronic hepatitis C has many features which suggest that this disease must be viewed not only as a viral disease, but also as a metabolic liver disease which implies: insulin resistance [(13)], high prevalence of steatosis [(14)]. **Hourigan et al** [(15)] found a significant relationship between hepatic fibrosis and steatosis, suggesting that in chronic HCV infection steatosis may play a role in disease progression.

Our results show that significant hepatic steatosis (affecting>33% of cells) is present in about 54% of studied chronic HCV patients.

Our results are much higher than a recent study conducted in our department on CHC patients [(16)] that showed significant steatosis (>33%) is present in only 20% of CHC patients after excluding obese patients (BMI >30 $Kg/m^{2)}$ and diabetic patients. This frequency of significant is higher than that reported in Greek patients with CHC genotype 4 where 26.4 % of them showed significant steatosis [(17)].

In the current study, patients with different severity of steatosis did not show significant difference in their mean age. This was in agreement with **El-Zayadi et al** [(18)] who demonstrated that age is not significantly correlated with steatosis among HCV genotype 4 infected patients. In our study, we found no relation between hepatic fibrosis and age, unlike **Hu et al** [(19)] who declared that older patients had advanced stages of fibrosis.

Our study showed a significant association between BMI and the severity of steatosis. This agrees with **Hu et al** [(19)] and **Negro and Sanyal** [(20)] who found that BMI plays an important role in steatosis in patients

with HCV. This contrast with **Adinolfi et al** [8] who found that steatosis was not significantly associated with BMI in the overall cohort study of HCV infected patients.

In our study, we found a significant relation between BMI and stages of fibrosis. And this agrees with **Hourigan et al** [15] and **Hu et al** [19].

We found that type 2 DM was present more in group 2 (47.4%) steatosis than in group 1 (18.2%), but with no statistically significant difference. **El-Zayadi et al** [18] also declared that DM was not significantly associated with hepatic steatosis in HCV genotype 4 patients. We as well as others, **Castera et al** [21] **and Negro and Sanyal** [20] also found a significant association between levels of serum triglycerides and the degree of steatosis in patients with HCV. This disagrees with **Hu et al** [22] who revealed in their cohort of patients with chronic hepatitis C, that hypertriglyceridemia was not significantly associated with hepatic steatosis.

In our study, we found a significant relationship between the serum triglycerides and fibrosis stage. This was in agreement with **Hu et al** [19] and in contrast to **Solis-Herruzo et al** [23], who failed to confirm this relation.

In the current study, we found that insulin resistance measured by HOMA-IR was significantly higher in chronic HCV patients than control, and it was significantly higher in group 2 steatosis than in group 1. Also, higher serum insulin level was found in more advanced steatosis than in milder group and controls. This was in agreement with **Cua et al** [11] **and Lawrence and Jacqueline** [24] who demonstrated that patients with HCV have more insulin resistance than those without. This also agrees with **Younossi et al** [25] who demonstrated that patients with HCV have more insulin resistance and poor response to treatment. In contrast to our study, **Muzzi et al** [26] delineated in their cohort study that the level of insulin resistance was not correlated with hepatic steatosis in HCV infected patients.

In the present study, no correlation was found between insulin resistance as measured by HOMA-IR and hepatic fibrosis in chronic HCV patients, and this conforms with **Grigorscu et al** [27] who revealed a lack of correlation between IR and fibrosis. In contrast to **D'Souza et al** [28] who reported that IR plays an important role in hepatic fibrosis in chronic HCV patient, irrespective of the genotype. Also, we found that BMI was an independent risk factor associated with stage 3 and 4 fibrosis, in agreement with **Hu et al** [19] who reported that both obesity and BMI were associated with stage 3 and 4 fibrosis.

In the current study, mean serum adiponectin level was significantly lower in patients than controls. Also, it was significantly lower in group 2 steatosis than group 1 steatosis. On the other hand, CHC patients show significantly higher TNF-α level than the control. Also, TNF-α was significantly more raised in group 2 steatosis than group 1 and hence, a significant positive correlation was found between TNF-α on one hand and the degree of steatosis, HOMA-IR and stage of fibrosis on the other hand. The same imbalance was also reported by **Durante-Mangoni et al** [29] who found that low level of adiponectin and elevated level of TNF-α were independently associated with grades of steatosis and HOMA-IR.

Unlike their intimate relation to hepatic steatosis, we did find that imbalance between serum adiponectin and TNF-α had a direct relationship to the progression of fibrosis, despite the elevated level of TNF-α in patients than in controls [30]. **Lu et al** [31] also found that serum level of adiponectin did not differ significantly between healthy subjects and patients with HCV infection.

Our work coincides with the work done by **Cua et al** [11] who failed to demonstrate the relation between serum leptin, adiponectin, IL-6 and TNF-α with portal/periportal inflammation, and these were not associated with steatosis grade or fibrosis stage.

In the present study, multivariate analysis of our data revealed that HOMA index (P<0.001) and TNF-α (P<0.03) are the most independent factors predicting hepatic steatosis in patients with HCV. Steatosis was not an independent factor associated with fibrosis, and only BMI (P<0.01) and triglycerides (P<0.03) were independently predict advanced fibrosis.

Our findings disagrees with **Rubbia-Brandt et al** [32] **and Cholet et al** [4] who reported a significant association between steatosis and high stage of fibrosis.

Our results show that steatosis was significantly associated with the presence of MS in CHC patients. This was also reported by **Grigorscu et al** [27] in patients with genotype 1.

This together with the absence of a significant association between viral load and degree of steatosis in our study strongly suggest that steatosis in the current series is due to metabolic origin.

Conclusion:

In conclusion, in patients with CHC in Upper Egypt, higher BMI, HOMA-IR, lower serum adiponectin and higher serum TNF-α and triglycerides were associated with HCV hepatic steatosis and metabolic syndrome, while higher BMI and serum triglycerides were associated with more advanced fibrosis stage.

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الملخص العربي

تعتبر مصر من أعلي دول العالم من حيث معدل الإصابة بالفيروس الكبدي المزمن (سي). و غالبا ما يصاحب هذه الإصابة حدوث تشحم و تليف في الكبد. ولابد من معرفة ما إذا كان حدوث هذا التشحم و التليف نتيجة للفيروس بذاته، أم أنه نتيجة لعوامل أيضية أخري. و لابد أيضا من تقييم تأثير مقاونة الأنسولين المصاحبة للإصابة و العوامل الأيضية علي مدى تشحم الكبد و تليفه، و معرفة العلاقة بين الاصابة بفيروي سي و المتلازمة الأيضية.

و لقد قامت هذه الدراسة علي 71 مريضا بافيروس الكبدي المزمن (سي)، بالإضافة إلي 12 من الأصحاء الذين لا يعانون من أمراض كبدية، و تم عمل جميع الفحوصات المعملية لهم و قياس معامل مقاومة الأنسولين، و عمل فحص بالموجات فوق الصوتية لهم، بالإضافة إلي أخذ عينة كبدية لقياس مدي التشحم و التليف المصاحب للإصابة.

وجدنا في هذه الدراسة أن التشحم موجود بدرجة عالية (>33%) في حوالي 54% من المرضي، و موجود بدرجة أقل (<33%) في حوالي 46% من المرضي. ووجدنا أن 21,12% من المرضي لديهم مراحل متقدمة من التليف (مرحلة ثالثة أو رابعة)، و 22,5 % لديهم مرحلة ثانية، و معظمهم (56%) لديهم مرحلة أولي من التليف.

و بدراسة العوامل المصاحبة لهذا الالتشحم و التليف، وجدنا ان التشخم يكون مصاحبا لإنخفاض نسبة الأديبونيكتين في الدم و إرتفاع نسبة عامل تنخر الأورام –ألفا، إرتفاع معامل كتلة الجسم، إرتفاع نسبة الدهون الثلاثية. و عند عمل التحليل متعدد العوامل وجدنا أن معامل مقاومة الأنسولين و عامل تنخر الأورام-ألفا هما أكثر العوامل التي تؤدي إلي تشحم الكبد في مرضي الفيروس الكبدي (سي) المزمن.

ووجدنا أيضا أن المتلازمة الأيضية في مرضي فيروس (سي) المزمن لها علاقة وثيقة الصلة. بإرتفاع نسبة التشحم و إرتفاع نسبة عامل تنخر الأورام –ألفا وإنخفاض نسبة الأديبونيكتين.

و عند دراسة تليف الكبد لدى هؤلاء المرضي، و عند عمل التحليل متعدد العوامل، وجدنا أن إرتفاع معامل كتلة الجسم و إرتفاع الدهون الثلاثية هما أكثر العوامل التي تؤدي إلي تليف الكبد في مرضي فيروس (سي).

<u>ومما سبق نستنج أن:</u>

إرتفاع كل من معامل معامل كتلة الجسم، معامل مقاومة الأنسولين، عامل تنخر الأورام- ألفا و الدهون الثلاثية، و إنخفاض نسبة الأديبونيكتين يكون مصاحبا لتشحم الكبد و المتلازمة الأيضية في مرضي فيروس (سي) المزمن، بينما يصاحب تليف الكبد في مرضي فيروس (سي) المزمن كل من إرتفاع معامل كتلة الجسم و الدهون.