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IMPACT OF INSULIN RESISTANCE AND SERUM ZINC ON RESPONSE TO PEG-INTERFERON/RIBAVIRIN COMBINATION THERAPY IN NON-DIABETIC PATIENTS WITH CHRONIC HEPATITIS C

By

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ABSTRACT

Background: Hepatitis C virus (HCV) infection is an important risk factor for insulin resistance (IR). IR, through different mechanisms, plays a role in the development of steatosis and its progression to steatohepatitis, cirrhosis and even hepatocellular carcinoma (HCC). In addition, IR has a role in impairing tumor necrosis factor (TNF) signaling cascade, which in turn blocks signal transducer and activator of transcription-1 (STAT-1) translocation and interferon stimulated genes production avoiding the antiviral effect of interferon

Objective: Evaluation of the prevalence of insulin resistance among chronic hepatitis C patients, and the impact of insulin resistance and serum zinc (Zn) on sustained virological response in non-diabetic, non-cirrhotic patients with chronic hepatitis C receiving combined pegylated Interferon and ribavirin therapy**.**

Patients and Methods: This was an observational and cross-sectional study with a prospective inclusion of data that was conducted in Tropical Medicine Department, Al-Azhar University Hospitals and Gastroenterology and Hepatology Departments, Police Forces Hospitals, during the period between 2013 and 2015.There were 205 chronic hepatitis C patients who fulfilled the inclusion criteria and index of insulin resistance measured by using homeostasis model assessment of insulin resistance (HOMA-IR) which was calculated by the formula: Fasting glucose (mg/dl) x fasting insulin (μU/ml) / 405.

Results: *HOMA-IR* among chronic hepatitis C patients was 53.2%. There were significant correlations between HOMA-IR and sustained virological response (SVR) achieved by pegylated interferon/ribavirin combination therapy. Patients with IR were more likely to have steatosis, higher grades of fibrosis and periportal necroinflamatory activity.

Conclusion: Serum zinc (Zn) has no impact on sustained virological response. The sustained virological response (SVR) rate in non insulin-resistant patients was better than in insulin-resistant patients after treatment using pegylated interferon/ribavirin combination therapy. Insulin-resistant patients had higher levels of HCV-induced liver fibrosis, steatosis and necroinflamatory activity, compared with patients without insulin resistance.

Key words: Insulin resistance, zinc, diabetes, peginterferon, ribavirin.

INTRODUCTION

IR is a complex pathophysiological condition where higher-than-normal concentrations of insulin are needed to maintain a normal glycemia and adequate glucose utilization in insulin target tissues

(Bloomgarden, 2007). The gold standard for the assessment of insulin resistance is the euglycemic hyperinsulinemic clamp technique. Another more applicable and also well-accepted method of measuring systemic insulin resistance is the HOMA-IR (homeostasis model assessment of insulin resistance). The HOMA-IR has been proved useful in measuring insulin sensitivity in euglycemic patients ***(Romero, 2006)***.

Hui et al. **(2003)** linked between HCV and insulin resistance (the primary pathogenetic factor of type 2 diabetes mellitus). Another prospective study comparing patients with CHB and CHC confirmed that IR is a specific feature of hepatitis C genotype 1 and 4 infection, but not CHB. HCV virus also has been shown to induce IR itself and thereby to promote hepatic inflammation and fibrosis ***(Moucari et al., 2008),*** and a lower SVR rate ***(Nasta et al., 2008)***. A third study found that HOMA-IR did not increase in people with CHB compared with matched healthy controls ***(Kumar et al., 2009).***

The improvement of IR after successful antiviral treatment (i.e. SVR) supports a direct role of HCV in IR development ***(Romero-Gomez et al., 2005).***It has been suggested that clinical application of pretreatment HOMA-IR made it possible to predict treatment outcome and determine treatment regimens ***(Dai et al., 2009)***. In addition, several studies demonstrate that IR is associated with decreased rates of SVR ***(Khattab et al., 2010)***. So, elucidation of the relationship between hepatitis C virus (HCV) and IR is of great clinical relevance ***(Yoneda et al., 2007)***.

Zinc supplementation relieves hepatic encephalopathy. In addition, oral administration of polaprezinc, a complex of zinc and l-carnosine, markedly improved necroinflammation in the liver of hepatitis C virus (HCV)-related chronic liver disease ***(Himoto et al., 2007)***. Serum Zn levels inversely correlate with the severity of hepatic fibrosis ***(Moriyama et al., 2006)***. Zn deficiency is also frequently observed in patients with chronic liver diseases including chronic hepatitis and liver cirrhosis ***(Stamoulis and Kouraklis, 2007)***.

AIM OF WORK

Evaluation of the prevalence of insulin resistance among chronic hepatitis C patients and the impact of insulin resistance and serum Zinc on sustained virological response in non-diabetic, non-cirrhotic patients with chronic hepatitis C receiving combined pegylated interferon and ribavirin therapy**.**

PATIENTS AND METHODS

This was an observational and cross-sectional study with a prospective inclusion of data that was conducted in Tropical Medicine Department, Al-Azhar University Hospitals, and Gastroenterology and Hepatology departments, Police Hospitals during the period between 2013 and 2015.

Two hundred and five non-diabetic male patients (ageing between 18-60 years) were selected from the outpatient clinics and were followed during and up to 6 months after the anti-HCV treatment.

The American Diabetes Association criterion of fasting glucose of ≥126 mg/dL**or** HbA1c ≥ 6.5 % was used to define diabetes ***(Diabetes Care, 2012)***.

Insulin resistance was determined for all patients using HOMA-IR formula: ***HOMA-IR = Fasting Glucose (mg/dl) x Fasting Insulin (µU/ml) / 405(Vasques et al., 2008)***.

Patients with HOMA-IR > 2 were labeled as insulin resistant consistent with previous studies ***(Romero-Gomez et al., 2005 and Vachon et al., 2011)***.

Zn deficiency was defined as serum Zn levels < 65 ?g/dl consistent with previous studies ***(Himoto et al., 2010)***.

Inclusion criteria

- The presence of HCV infection depending on the presence of anti-HCV antibody and detectable HCV-RNA by PCR.
- Patients with hemoglobin ≥ 13 g/dl, platelets >100,000/mm^3, and leucocytic count ≥ 3.700/mm^3.
- Patients with body mass index < **30**.
- All patients were informed by the nature of the study and informed written consents were obtained.

Exclusion criteria

- Diabetes mellitus (fasting glucose ≥ 126 mg/dL or HbA1c ≥ 6.5 %).
- Patients co-infected with HBV, HIV or bilhariziasis (bilharzial antibody test to be negative).
- Patients showed evidence of liver cirrhosis or other liver diseases by biopsy (steatosis and steatohepatitis were not excluded).
- Patients with decompensated liver disease (ascites, bleeding varices, or encephalopathy).
- Patients treated previously for HCV, alcohol use ≥ 50 g/day, or with medical problems that impair their ability to participate in the study.
- Chronic renal disease.
- Pregnant women.
- Auto-immune disorders, e.g. auto-immune hepatitis, SLE.

All patients were subjected to the following evaluation before starting treatment:

1. Full history taking and thorough clinical examination including anthropometric measurements (e.g. weight, height, BMI).
2. Quantitative real-time PCR for HCV-RNA (Taqman method, Q1A amp viral RNA, Mini Kit 50, Cat No 52904, Beckman Caulter, USA).
3. Liver biopsy and Metavir scoring.
4. Complete blood count (CBC), liver profile including ALT, AST, serum bilirubin, albumin, alkaline phosphatase, prothrombin time, prothrombin concentration and INR.
5. Alpha feto-protein in blood.
6. TSH and Creatinine.
7. Fasting glucose and insulin to calculate insulin resistance (HOMA-IR).
8. Serum Zn.
9. Lipid profile (total cholesterol, HDL, LDL and TGs).
10. ECG.

During the treatment period, the patients were followed by the following investigations:

1. CBC, creatinine, bilirubin, ALT and AST every month.
2. Quantitative real-time PCR for HCV-RNA at 12, 24 and 48 weeks of

treatment and at 6 months after end of treatment for SVR.

Statistical Methodology: IBM SPSS statistics V. 23.0, IBM Corp., USA, 2015, was used for data analysis. Data were expressed as Mean±SD for quantitative parametric measures in addition to Median Percentiles for quantitative non-parametric measures and both number and percentage for categorized data.

The following tests were done:

1. Comparison between two independent mean groups for parametric data using Student t test.

2. Comparison between two independent groups for non-parametric data using Wilcoxon Rank Sum test.

3. Ranked Sperman correlation test to study the possible association between each two variables among each group for non-parametric data.

4. Chi-square test to study the association between each 2 variables or comparison between 2 independent groups as regards the categorized data.

► P value < 0.05 was considered significant

► Multi-Regression analysis was used to search for a panel (independent parameters) that can predict the target parameter (dependent variable). By using stepwise multi-regression analysis, parameters among these panels can be sorted according to their sensitivity to discriminate.

RESULTS

The study was conducted on 205 patients diagnosed as chronic HCV, based on history, clinical examination, positive anti-HCV antibody test, detectable HCV-PCR and liver histology suggestive of chronic virus C hepatitis. According to the HOMA-IR, enrolled patients were classified into two groups:

Group 1(non insulin-resistant; non-IR): This group included 96 patients (all were men; mean age of 44.4 ± 4.8 years) with HOMA-IR ≤ 2.

Group 2 (insulin-resistant; IR): This group included 109 patients (all were men; mean age of 43.1 ± 5.2 years) with HOMA-IR > 2.

Out of 205 enrolled patients, 109 patients (53.2%) had HOMA-IR > 2 ***(Table 1)***.

Table (1): Prevalence of HOMA-IR among studied patients.

Studied patients	*IR patients (HOMA-IR>2)*	*% of IR patients*
205	109	53.2%

There were significant higher levels of total cord bilirubin, total serum bilirubin and retics in group 1 than group 2 and no significant difference as regard other laboratory data (Table 2).

Table (2): Comparison of SVR between IR and non-IR patients.

SVR \ HOMA		N-IR	IR > 2	Total	P
-ve PCR	Count	68	60	128	< 0.05
	%	70.8%	55%	62.4%	
+ve PCR	Count	28	49	77	
	%	29.2%	45%	37.6%	
Total	Count	96	109	205	
		100%	100%	100%	

There was highly statistical significant correlation between IR and non-IR patients regarding the median value of pretreatment ALT that was higher in non-IR versus IR patients. There was significant statistical correlation between IR and non-IR patients regarding the rate of decrease in ALT values (dC) during treatment (i.e. normalization of ALT) that was higher in non-IR group (dC; -0.2670) versus IR group (dC; -0.0925) (Table 3).

Table (3): Comparison between the ALT in IR versus non-IR patients (using Wilcoxn Rank Sum Test).

Parameters \ Statistics		n	Mean	SD	p
ALT.0	G 1 (N-IR)	96	56	31	<0.01
	G 2 (IR)	109	54	11	
ALT.4	G 1 (N-IR)	96	44	11.5	0.062
	G 2 (IR)	109	45	22	
ALT.12	G 1 (N-IR)	96	45	22	<0.05
	G 2 (IR)	109	43	3	
ALT.24	G 1 (N-IR)	88	43	7	<0.01
	G 2 (IR)	105	45	15	
ALT.48	G 1 (N-IR)	84	47	9	0.851
	G 2 (IR)	97	43	13	
ALT.dC	G 1 (N-IR)	96	-0.2670	0.2083	<0.05
	G 2 (IR)	109	-0.0925	0.3973	

G1: group 1 , G2: group2, IR: insulin resistance, N-IR; non insulin-resistance, ALT; Alanine amino transaminase ALT.0; ALT before treatment, ALT; ALT at week 4 of treatment, ALT.12; ALT at week 12 of treatment, ALT.24; ALT at week 24 of treatment, ALT.48; ALT at week 48 of treatment, ALT.dC; statistical change of ALT value during treatment.

There was significant statistical difference between IR and non-IR patients regarding the rate of decrease in platelets (dC) during treatment that was higher in IR (dC; -0.3550) versus non-IR patients (Table 4).

Table (4): Comparison between platelets in IR versus non-IR patients (using Wilcoxn Rank Sum Test).

Parameters \ Statistics		*n*	*Mean*	*SD*	*p*
Platelets.0	***G 1 (N-IR)***	*96*	*329*	*25*	***0.155***
	G 2 (IR)	*109*	*324*	*30*	
Platelets .4	***G 1 (N-IR)***	*96*	*249*	*41*	***<0.01***
	G 2 (IR)	*109*	*198*	*89*	
Platelets .12	***G 1 (N-IR)***	*96*	*222.5*	*54*	***0.072***
	G 2 (IR)	*109*	*210*	*55*	
Platelets .24	***G 1 (N-IR)***	*88*	*214.5*	*25.5*	***0.626***
	G 2 (IR)	*105*	*214*	*51*	
Platelets .48	***G 1 (N-IR)***	*84*	*209*	*80*	***<0.01***
	G 2 (IR)	*97*	*205*	*13*	
Platelets .dC	***G 1 (N-IR)***	*96*	*-0.2840*	*0.2966*	***<0.05***
	G 2 (IR)	*109*	*-0.3550*	*0.2088*	

Platelets.0; platelets before treatment, platelets.4; platelets at week 4 of treatment, platelets.12; platelets at week 12 of treatment, platelets.24; platelets at week 24 of treatment, platelets.48; platelets at week 48 of treatment, Platelets.dC; statistical change of platelets value during treatment.

There was highly statistical significant correlation between IR and non-IR patients regarding the rate of decrease in absolute neutrophilic count (dC) during treatment that was higher in IR (dC; -0.225) versus non-IR patients (Table 5).

Table (5): Comparison of ANC between IR and non-IR patients (using Wilcoxn Rank Sum Test).

Parameters \ Statistics		*n*	*Mean*	*SD*	*p*
ANC.0	***G 1 (N-IR)***	*96*	*2.8*	*0.7*	***0.061***
	G 2 (IR)	*109*	*2.6*	*0.5*	
ANC.4	***G 1 (N-IR)***	*96*	*2.6*	*1*	***0.062***
	G 2 (IR)	*109*	*2.3*	*1.3*	
ANC.12	***G 1 (N-IR)***	*96*	*2.4*	*0.675*	***0.326***
	G 2 (IR)	*109*	*2.4*	*0.6*	
ANC.24	***G 1 (N-IR)***	*88*	*2.1*	*o.7*	***0.424***
	G 2 (IR)	*105*	*2.3*	*0.8*	
ANC.48	***G 1 (N-IR)***	*84*	*2.2*	*1*	***<0.01***
	G 2 (IR)	*97*	*1.9*	*0.8*	
ANC.dC	***G 1 (N-IR)***	*96*	*-0.1*	*0.1943*	***<0.01***
	G 2 (IR)	*109*	*-0.225*	*0.225*	

ANC; Absolute neutrophilic count, ANC.0; ANC before treatment, ANC.4; ANC at week 4 of treatment, ANC.12; ANC at week 12 of treatment, ANC.24; ANC at week 24 of treatment, ANC.48; ANC at week 48 of treatment, ANC.dC; statistical change of ANC value during treatment.

There was a highly significant statistical difference between both groups regarding steatosis (Table 6).

Table (6): Comparison between the two studied groups (IR and non-IR) as regards steatosis.

HOMA / *Steatosis*		*G 1 (N-IR)*	*G 2 (IR)*	*Total*	*P*
5%	*Count*	*16*	*36*	*52*	***<0.01***
	%	*16.7%*	*33.0%*	*25.4%*	
10%	*Count*	*4*	*25*	*29*	
	%	*4.2%*	*22.9%*	*14.1%*	
15%	*Count*	*4*	*12*	*16*	
	%	*4.2%*	*11.0%*	*7.8%*	
20%	*Count*	*0*	*8*	*8*	
	%	*0.0%*	*7.3%*	*3.9%*	
None	*Count*	*72*	*28*	*100*	
	%	*75.0%*	*25.7%*	*48.8%*	
Total	*Count*	*96*	*109*	*205*	
	%	*100%*	*100%*	*100%*	

There was a highly significant statistical difference between both groups regarding fibrosis (Table 7).

Table (7): Comparison between the two studied groups (IR and non-IR) as regards fibrosis.

HOMA / *Fibrosis*		*G 1 (N-IR)*	*G 2 (IR)*	*Total*	*P*
F1	*Count*	*68*	*28*	*96*	***<0.01***
	%	*70.8%*	*25.7%*	*46.8%*	
F2	*Count*	*20*	*61*	*81*	
	%	*20.8%*	*56.0%*	*39.5%*	
F3	*Count*	*8*	*20*	*28*	
	%	*8.3%*	*18.3%*	*13.7%*	
Total	*Count*	*96*	*109*	*205*	
	%	*100%*	*100%*	*100%*	

F1; fibrosis grade1, F2; fibrosis grade2, F3; fibrosis grade3.

There was highly significant statistical difference between both groups regarding necroinflamatory activity (Table 8).

Table (8): Comparison between the two studied groups (IR and non-IR) as regards necroinflamatory activity.

HOMA / *Necro-inflamatory activity*		*G 1 (N-IR)*	*G 2 (IR)*	*Total*	*P*
A1	*Count*	*52*	*41*	*93*	***<0.01***
	%	*54.2%*	*37.6%*	*45.4%*	
A2	*Count*	*44*	*56*	*100*	
	%	*45.8%*	*51.4%*	*48.8%*	
A3	*Count*	*0*	*12*	*12*	
	%	*0.0%*	*11.0%*	*5.9%*	
total	*Count*	*96*	*109*	*205*	
	%	*100%*	*100%*	*100%*	

A1; necro-inflamatory activity grade1, A2; necro-inflamatory activity grade2, A3; necro-inflamatory activity grade 3.

Stepwise multi-regression analysis of laboratory predictors of SVR showed that HOMA-IR (odds ratio: 3.013, P = 0.003) was independent factor associated with SVR with highly significant statistical difference (Table 9).

Table (9): Stepwise multi-regression analysis of laboratory predictors of SVR

Statistics / *Item*	*Reg. Coef*	*T*	*P*	*F-Ratio*	*P*
(Constant)	*0.964*	*4.612*	*0*	***13.023***	***<0.01***
HOMA.IR	*0.04*	*3.013*	*0.003*		

DISCUSSION

Hepatitis C virus (HCV) infection is one of the main causes of chronic liver disease worldwide. Many viral and host factors have been implicated in disease progression and/or response to antiviral treatment. Among those factors insulin, resistance (IR) is noteworthy. Different studies have demonstrated an association between HCV infection and increase in IR prevalence ***(Parise & Oliveira, 2007; Moucari et al., 2008; del Campo, 2009 and Romero-Gomez, 2011)***.In hepatitis C, IR is related to the presence of steatosis, faster fibrosis progression and increased risk of progression to cirrhosis and hepatocellular carcinoma ***(Taura et al., 2006; Moucari et al., 2008 and Veldt et al., 2008)***. The observation that successful antiviral treatment (SVR) improved IR supports a direct causal role of HCV in IR development ***(Romero-Gomez et al., 2005).*** It has been suggested that clinical application of pretreatment HOMA-IR made it possible to predict treatment outcome and determine treatment regimens ***(Dai et al., 2009)***. In addition, several studies demonstrate that IR is

associated with decreased SVR ***(Khattab et al., 2010)***.

In our study, 53.2% of CHC patients were found to be insulin resistant, which is compatible with ***Kiran et al., (2013)*** who reported IR prevalence of 51%, and ***Hsu et al., (2008)*** who reported a rate of (56.1%). However, our results were much higher than that reported by ***Hao-Chun Huang et al. (2011)*** who reported a prevalence rate of 39.2%, and ***Souza et al. (2011)*** who reported a prevalence rate of 27% using cut-off value of HOMA-IR > 2.5. Other studies also reported lower rates of insulin resistance ***(Moucari et al., 2008)***. This difference in prevalence may be explained by different cut-off values of HOMA-IR.

Our study showed that the overall SVR was 62.4%. SVR of non-IR patients (HOMA-IR<2) was 70.8%, while SVR of insulin-resistant patient (HOMA-IR>2) was (55%) with significant statistical difference **.**This is in agreement with ***Khattab et al, (2010)*** who reported that the overall SVR rate among Egyptian CHC patients was 60.3%, SVR rate of insulin-resistant patients (HOMA-IR<2) was 88.6%, whereas that in insulin-resistant patients (4 > HOMA-IR > 2) was 56 % , and SVR of insulin-resistant patients with HOMA-IR > 4 was 14.2%.

Our study was also in agreement with ***Eslam et al. (2011)*** who concluded that the increase in the HOMA-IR index was associated with lower therapeutic response in subjects infected by chronic HCV. However, ***Eslam et al. (2012)*** demonstrated that SVR rate was significantly reduced among patients with HOMA-IR≥2 for each genotype analyzed (G1, G3, and G4). This difference was maintained even when different cut-off values of HOMAIR were used to define IR (>3 and >4).

Our study showed that stepwise multi-regression analysis of laboratory predictors of SVR showed that HOMA-IR was an independent factor associated with SVR with highly significant statistical difference. This is in consistent with ***Khattab et al. (2010)*** who reported that fibrosis, HOMA-IR and viral load were independent factors associated with SVR. ***Romero-Gomez et al. (2005)*** showed that HOMA-IR, degree of fibrosis, and HCV genotype are independent predictors of the response to anti-HCV therapy.

Our study found that chronic HCV was not associated with zinc deficiency. This is in parallel with ***Mohammed et al., (2014)*** who found that serum Zn levels were similar between the chronic HCV patients and controls.

A link between steatosis and IR has already been reported in previous studies ***(Camma et al., 2006 and Conjeevaram et al., 2007)*** and was attributed to host metabolic disorders or due to HCV infection. In addition, ***Kawagutchi et al. (2004)*** reported that HCV infection changes a subset of hepatic molecules regulating glucose metabolism. A possible mechanism is that HCV core-induced suppressor of cytokine signaling (SOCS) 3 promotes proteosomal degradation of IR substrates 1 and 2. Furthermore, ***Akuta et al. (2009)*** have shown that amino acid substitutions in the HCV core region are the important predictor of severe insulin resistance in patients without cirrhosis and DM.

In our study, we found that among non-IR patients there were 75% of

patients showing no steatosis and 16.7% of patients showing 5% steatosis, 4.2% showing 10% steatosis, 4.2% of the patients showing 15% steatosis and there were no patients showing 20% steatosis. Among IR patients there were 48.8% showing no steatosis and 33% showing 5% steatosis, 22.9% showing 10% steatosis, 11% showing 15% steatosis and 7.3% showing 20% steatosis with highly significant statistical difference. This was in accordance with ***Souza et al., (2011)*** who reported that patients with IR were more likely to have steatosis, higher significant grades of fibrosis and periportal necroinflamatory activity. Furthermore, patients with IR had higher significant rates of advanced liver fibrosis and a tendency towards higher significant rates of periportal necroinflammatory activity ≥ 2. This was also, consistent with ***Kiran et al., (2013)*** who reported patients with insulin resistance showed a significantly higher mean degree of steatosis. Our finding also was compatible with ***Ahmed et al., (2011)***, who found in multivariate analysis that only insulin resistance was the significant and independent predictor of hepatic steatosis among Egyptian CHC patients. However our data doesn't cope with ***Kato et al., (2015)*** who were unable to find association between insulin resistance and hepatic steatosis. This may be due to different genotypes of HCV.

In our study we found that among non-IR patients, there were 70.8% of patients showing fibrosis grade I, 20.8% showing fibrosis grade II and 8.3% showing fibrosis grade III. Among IR patients there were 25.7% of patients showing fibrosis grade I, 56% showing fibrosis grade II and 18.3% showing fibrosis grade III with highly significant statistical difference. This was in agreement with ***Kiran et al., (2013)*** who reported that patients with IR (HOMA-IR ≥ 2) had a higher prevalence of significant fibrosis defined as Metavir $\geq$ F2 when compared to those without IR. Our results were also comparable with past studies demonstrating a relationship between insulin sensitivity and fibrosis score in non-cirrhotic, non-diabetic patients with chronic HCV ***(Souza et al., 2011 and Ziada et al., 2012)***.

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تأثير مقاومة الإنسولين و مستوي الزنك علي الإستجابة لعلاج الإلتهاب الكبدي الفيروسي المزمن (سي) المكون من الإنترفيرون والريبافيرين في المرضي الغير مصابين بمرض البول السكري

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خلفية البحث: تُعتبر الإصابة بالفيروس الكبدي "سي" أحد أهم أسباب الإلتهاب الكبدي المزمن علي مستوي العالم .يتنوع التأثير الفيروسي علي الكبد، بدايةً من مجرد تغييرات طفيفة في أنسجة الكبد ثم تنتهي بالتليف الكبدي و سرطان الكبد.

وقد ربط الباحثين بين الإلتهاب الكبدي الفيروسي "سي" و المقاومة الداخلية للإنسولين. وقد لوحظ تحسن المقاومة الداخلية للإنسولين بعد نجاح العلاج ضد الفيروس الكبدي "سي" و ثبت وجود علاقة سببية مباشرة بين الفيروس و المقاومة الداخلية للإنسولين. وهناك دراسات أخري بيَّنَت وجود نقص عنصر الزنك من الجسم في مرضي الإلتهاب الكبدي الفيروسي المزمن "سي" و مرضي التليف الكبدي.

الهدف من البحث: توضيح مدي أنتشار المقاومة الداخلية للإنسولين ونقص عنصر الزنك في مرضي الإلتهاب الكبدي الفيروسي "سي" المُزمن، و مدي تأثير ذلك علي الإستجابة للعلاج بعقاري الإنترفيرون والريبافيرين.

المرضي و طرق البحث: أُجرِيَت هذه الدراسة في مستشفيات جامعة الأزهر و مستشفي هيئة الشرطة في الفترة من ٢٠١٣إلي ٢٠١٥، وقد ضَمَّت الدراسة ٢٠٥ مريض من مرضي الإلتهاب الكبدي الفيروسي "سي" المترددين علي عيادة الفيروسات الكبدية و الذين تنطبق عليهم شروط العلاج بالإنترفيرون طويل المفعول طبقاً للوائح اللجنة القومية لمكافحة و علاج فيروس "سي" في مصر، و تنطبق عليهم أيضا شروط البحث من حيث عدم وجود تليف كبدي أو سمنة (معامل كتلة الجسم <٣٠) أو مرض البول السكري (سكر صايم <١٢٦ أو هيموجلوبين سكري <٦,٥٪).

النتائج:

١- لا يوجد نقص في الزنك بين مرضي الإلتهاب الكبدي الفيروسي "سي".
٢- عدد المرضي الذين لديهم مقاومة داخلية للإنسولين يبلغ ٥٣,٢٪ من بين المرضي المصابين بالإلتهاب الكبدي الفيروسي "سي" المزمن.
٣- هناك علاقة ذات دلالة إحصائية هامة تفيد تأثير المقاومة الداخلية للإنسولين السلبي علي الإستجابة للعلاج بعقار الإنترفيرون.

الإستنتاج: وجود مقاومة داخلية للإنسولين في مرضي الإلتهاب الكبدي الفيروسي "سي" المزمن يوصي بعلاجها قبل البدء في علاج الفيروس الكبدي "سي".