Hepatitis C virus (HCV) infection as a risk factor of atherosclerosis in patients with end stage renal disease (ESRD) on regular hemodialysis in Al-Gharbiyah Governorate in Egypt

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Abstract: The relation between HCV infection and kidney disorders is well recognized. Hepatitis C virus patients are more likely to have carotid atherosclerosis plaques as compared to HCV negative individuals. This study assessed the relation of HCV infection with atherosclerosis in hemodialysis patients. Forty patients with ESRD on regular hemodialysis were included in the study. Patients were divided into 2 groups. Group 1, included 20 patients known to be HCV infection, but no hepatitis B virus (HBV) infection, and Group 2 which included 20 patients known to have neither HCV nor HBV infection. All subjects were subjected to full clinical evaluation. Laboratory investigations included: complete blood count, and levels of: fasting plasma glucose, alanine transaminase (ALT), aspartate transaminase (AST), total serum bilirubin, serum albumin, lipid profile, Serum calcium, serum phosphorus, parathormone hormone (PTH), prothrombin time(PT), partial thromboplastin time (PTT), international normalizing ratio (INR), serum creatinine, blood urea, blood urea nitrogen (BUN), C- reactive protein (CRP), HCV antibodies, polymerase chain reaction (PCR) for HCV, and hepatitis B virus surface antigen (HBSag). Duplex study of both carotid arteries was carried-out. The study showed that serum levels of ALT, AST, LDL-Ch and PTH were significantly higher in HCV positive patients undergoing hemodialysis (P= 0.036, 0.042, 0.018 and 0.009 respectively), and there was significantly higher carotid atherosclerotic diameters among HCV positive patient as proved by carotid duplex study. **In conclusion:** we conclude that HCV infection in hemodialysis patients increases the risk of atherosclerosis as proved by carotid duplex.
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1. Introduction:

More than 50 % of ESRD patients die from cardiovascular diseases (**Collins, 2003**). Arteries of ESRD patients are affected by atherosclerosis and by large artery (media and intima) calcifications (**Ballanti *et al.*, 2011**). Many risk factors have been identified, they include traditional risk factors known from the non-ESRD population (diabetes mellitus, smoking, hypertension etc.), but also factors specific for renal failure, such as increased phosphate concentrations, inflammation, oxidative stress, malnutrition and increased serum levels of circulating ADMA (asymmetric di-methyl-arginine, endogenous inhibitor of nitric-oxide synthase). Despite these findings, the use of traditional risk scoring underestimates atherosclerosis burden (**Coll *et al.*, 2010**). Carotid ultrasonography (US) is one of the most used imaging techniques for the assessment of atherosclerosis, and it is increasingly applied in patients with ESRD and in CKD in general. Carotid intima-media thickness (IMT), the number of plaques and indicators of arterial remodeling, are regarded as major US indicators for the staging of the atherosclerosis process (**Roman *et al.*, 2006**).

Hepatitis C virus usually spreads by sharing infected needles with a carrier, from receiving infected blood, and from accidental exposure to infected blood. Some people acquire the infection through non-parenteral means that have not been fully defined, as sexual transmission in persons with high risk behaviors, although sexual transmission of HCV is less common than that of HBV and HIV (**Ansar and Kooloobandi, 2002**). Hemodialysis risk factors include blood transfusions, the duration of hemodialysis, and the prevalence of HCV infection in the dialysis unit, and the type of dialysis. The risk is higher with in hospital hemodialysis versus peritoneal dialysis. Contaminated medical equipments, traditional medicine rites, tattooing, and body piercing are considered rare transmission routes. There is some risk of HCV transmission for health care workers after unintentional needle-stick injury or exposure to other sharp objects (**Alter, 2007**).

Hepatitis C virus infection is a disease with a significant global impact. According to the World Health Organization there are 130-170 million people infected with HCV. There are considerable regional differences. Egypt has the highest hepatitis C virus (HCV) prevalence in the world (14.7%) (**Mohamoud *et al.*, 2013**), the prevalence of HCV antibodies in hemodialysis patients ranging from 52.3 to 82.3% (**Afifi, 2008**).

A Previous work by **Aslam *et al.*, 2010,** demonstrated that HCV infection was associated with the presence of carotid atherosclerotic plaques which might indicate increased risk of atherosclerosis in patients with HCV infection.

Because of increased risk of hepatitis C virus infection in Egyptian patients on hemodialysis, and because of well-known increased cardiovascular risk in patients with ESRD, we studied the relation of HCV infection in patients with ESRD in Al-Gharbiyah Governorate in Egypt.

2. Patients and methods:

Patients:

The present study included 40 patients with ESRD on regular hemodialysis with ages ranged between 20-65 years. Patients were selected from hemodialysis unit in Tanta University Hospital. All the patients were informed about the aim of the study and a written consent was taken from the patients and study was approved by the research ethical committee of Tanta Faculty of Medicine.

Study Design:

Twenty eight male and twelve non pregnant female patients known to have ESRD and are on regular hemodialysis were included in 2 groups:

Group 1:

Included 20 patients (14 males and 6 females) known to have HCV infection and no HBV infection.

Group 2:

Included 20 patients (14 males and 6 females) known to have neither HCV nor HBV infection.

After investigations we divided patients into group (A) which included atherosclerotic patients who had signs of atherosclerosis by carotid duplex study and group (B) of non atherosclerotic patients.

Inclusion criteria:

Patients on regular hemodialysis for more than 3 months.

Exclusion criteria:

1. Patients who are suffering from Diabetes Mellitus.
2- Patients with other traditional risk factors of atherosclerosis.
2. Patients who are receiving cholesterol lowering medications.
3. Patients who had history of carotid artery surgery or angioplasty.
4. Patients who are suffering from neck trauma or surgery affecting sonographic visualization of Carotid arteries.

All patients were subjected to the following:

1. Medical History:

Including age, sex, and residence, level of education, occupation, marital state and special habits.

2. Physical examination:

Including revision of all systems and three consecutive measurements of sitting blood pressure were recorded. Systolic and diastolic blood pressures were computed as the mean of the three measurements.

3. Anthropometric measurements:

Weight was measured to the nearest 0.5 kg and height to the nearest 1.0 cm. BMI was calculated as body weight in kilograms divided by the square of height in meters (kg/m^2).

4. Laboratory investigations:

Complete blood count, and levels of: fasting plasma glucose (FPG), ALT, AST, total serum bilirubin, serum albumin, serum triglycerides, total serum cholesterol, high density lipoprotein cholesterol (HDL-Ch),low density lipoprotein cholesterol (LDL-Ch), Serum calcium, serum phosphorus, parathormone hormone (PTH), prothrombin time (PT), partial thromboplastin time (PTT), international normalizing ratio (INR), serum creatinine, blood urea, blood urea nitrogen (BUN), C- reactive protein (CRP), HCV antibodies, polymerase chain reaction (PCR) for confirmation of HCV infection, and hepatitis B virus surface antigen (HBSag).

5. Radiological investigations:

All patients were subjected to duplex study of both Carotid arteries with measurement of intima-media thickness.

3. Results:

Table (1) shows that there was no significant difference between studied groups regarding age, BMI, systolic and diastolic BP, pre and post dialysis blood urea level, serum creatinine level and BUN level ($p > 0.05$).

In table (2)we can see that serum levels of ALT, AST and PTH were significantly higher in patients with HCV infection ($P = 0.036$, $p = 0.042$ and $p = 0.009$ respectively), but there was no significant difference between hepatitis C infected patients and non infected patients regarding levels of FPG, serum albumin, total serum bilirubin, PT, PTT, INR, CRP, blood hemoglobin (HB), packed cell volume (PCV), platelet count and total leucocytic count (TLC) ($P > 0.05$). Also, there was no significant difference in serum level of phosphorus and ionized calcium between both groups ($p < 0.05$). Also, serum level of LDL-Ch. was higher in patients with hepatitis C virus infection than those with no hepatitis C virus infection (98±34.8 and 87.1+12.5 respectively) ($p = 0.018$), but there was no significant difference in serum level of total cholesterol, HDL-Ch and triglycerides between both group ($P > 0.05$).

As seen in table (3), the number of atherosclerotic patients was higher in hepatitis C positive patients than in hepatitis C negative [16

(80%) and 7 (35%) respectively] (p=0.001). Also, table (3) shows the diameter of atherosclerosis among atherosclerotic positive patients of both groups which revealed a significantly higher longitudinal and transverse diameters of atherosclerosis in right common carotid artery in HCV positive patients (1.35+0.40 and 1.24+1.18 respectively) than those with no hepatitis C virus infection (1.11+0.34 and 1.05+0.27 respectively) (p= 0.048 and 0.046 respectively). Also, there was significantly higher longitudinal and transverse diameters of atherosclerosis in left common carotid artery in HCV positive patients (1.27+0.30 and 1.20+0.26 respectively) than those with no hepatitis C virus infection (1.01+0.25 and 1.0+0.23 respectively) (p= 0.042 and 0.038 respectively). On the other-hand, there was no significant difference between longitudinal and transverse diameters of atherosclerosis between right and left common carotid arteries within each group (P> 0.05).

Table (1): demographic, clinical data and dialysis effect on renal function tests of both groups

Parameter	G1	G2	t. test	*P* value
BMI	23.41±2.99	24.41±3.25	0.325	0.471
Age	41.62±4.95	44.36±3.25	0.530	0.258
Systolic BP	116.35±7.52	120.25±3.63	0.365	0.634
Diastolic BP	83.15±6.52	85.36±7.52	0.325	0.563
Blood urea				
Predialysis mean± SD	109.1±33.3	121.9±34.3	1.325	0.128
Postdialysis mean± SD	29.6±18.7	44.8±21.6	1.63	0.250
t. test	16.385	9.362		
P value	0.001*	0.001*		
Serum creatinine				
Predialysis mean± SD	8.39±2.40	9.07±3.1	0.365	0.241
Postdialysis mean± SD	2.90±1.55	3.87±2.1	0.241	0.528
t. test	7.241	9.362		
p. value	0.001*	0.001*		
BUN				
Predialysis mean± SD	50.7±14.3	59.6±16.2	2.951	0.074
Postdialysis mean± SD	16.8±8.4	21.1±11.6	1.900	0.085
t. test	9.362	7.956		
p. value	0.001*	0.006*		

Table 2: base-line laboratory findings of both groups

parameter		**G1**	**G2**	**t. test**	***P* value**
SGOT (AST)(u/L)	Range	12-102	9-51	5.326	0.042*
	Mean ±SD	39.2±18.3	25.8±12.1		
SGPT (ALT) (u/L)	Range	10-148	10-75	3.253	0.036*
	Mean ±SD	47.4±13.5	29.8±11.3		
S.ALB (g/dl)	Range	3.5-5.1	3.3-5	1.253	0.529
	Mean ±SD	4.43±0.43	4.29±0.37		
S.BIL	Range	0.9-1.1	0.8-1	0.362	0.225
	Mean ±SD	0.87±0.05	0.82±0.06		
Prothrombin time	Range	13-48.3	13-19.8	1.635	0.095
	Mean ±SD	17.1±1.11	13.7± 1.67		
Prothrombin activity	Range	30-100	47.5-100	0.253	0.639
	Mean ±SD	86.63± 32.43	91± 33.53		
INR	Range	1-7.1	1-1.89	1.325	0.969
	Mean ±SD	1.37± 0.63	1.11± 0.21s		
PTT	Range	27.4-120	28.8-51.4	1.635	0.852
	Mean ±SD	42.93± 21.33	37.29± 5.33		
HB%	Range	8-13.6	7.2-14.5	1.277	0.265
	Mean ±SD	10.09+1.60	10.70±1.82		
RBCs	Range	2.74-5.21	2.74-5.44		

parameter		G1	G2	t. test	*P* value
	Mean ±SD	3.69±0.75	3.85±0.67	0.501	0.483
Platelet	Range	60000-292000	70000-344000		
	Mean ±SD	166100±5145.3	176350±6145.2	0.327	0.571
TLC	Range	3400-14700	3000-9900		
	Mean ±SD	6480±2623.2	6005±2312.3	0.243	0.625
FBS	Range	50-113	55-110		
	Mean ±SD	86± 14.4	84.9± 14.7	0.158	0.574
S.PHOSPHORUS(mg/dl)	Range	4.2-7.3	3.3-11.2		
	Mean ±SD	5.37± 0.95	5.56± 1.74	0.172	0.325
S.ionized calcium (mg/dl)	Range	0.73-1.13	0.69-0.98		
	Mean ±SD	0.89± 0.11	0.86± 0.07	0.968	0.338
S.PTH (pg/ml)	Range	38.5-2502	17.7-1285		
	Mean ±SD	500.4± 125.3	272.2± 96.6	6.325	0.009*
Cholesterol (mg/dl)	Range	103-244	73-280	0.169	0.683
	Mean ±SD	159.2±36.4	153.7±48.1		
TGS(mg/dl)	Range			0.019	0.890
	Mean ±SD	148.9±19.3	153.2±35.6		
LDL(mg/dl)	Range	50-172	30-182	3.252	0.018*
	Mean ±SD	98±34.8	87.1±12.5		
HDL(mg/dl)	Range	24-57	25-53	0.915	0.345
	Mean ±SD	35.8±8.63	38.3±8.22		

In table (4) we can find a significantly higher serum level of PTH in atherosclerosis positive patients (23 patient) than atherosclerosis negative patients (13 patients) (452.6±69.3 and 258.3±19.5 respectively) (*P*= 0.028). While; age, BMI, systolic blood pressure, diastolic blood pressure, HB, PCV, platelet count, TLC, total serum bilirubin level, serum albumin level, ALT, AST, PT, PTT, INR, FPG and serum levels of phosphorous and calcium were not significantly different between atherosclerosis positive and atherosclerosis negative patients (p> 0.05).

Table (5) shows a comparison between atherosclerosis positive patients (23patients) and atherosclerosis negative patients (17 patients) as regard lipid profile which revealed a significantly higher serum LDL-Ch level in atherosclerosis positive group than in atherosclerosis negative group (88.42+15.28 mg/dl and 62.35+17.5 mg/dl respectively) (p=0.018). Similarly; total serum cholesterol level was significantly higher in patients with atherosclerosis than those without atherosclerosis (151.6+36.25 mg/dl and134.52+26.52 mg/dl respectively) (p=0.02). While; there was no significant difference between atherosclerosis positive patients and atherosclerosis negative patients in relation to serum levels of triglycerides and HDL-Ch (p> 0.05).

Table (4): findings of carotid duplex study of both groups

group		Presence of atherosclerosis			
		Yes	no		
Hepatitis C positive (G1)		16 (n)	4 (n)		
		80%	20%		
Hepatitis C negative (G2)		7(n)	13(n)		
		35%	65%		
X2		6.698			
P		0.001*			
Diameter of atherosclerotic area					
Longitudinal diameter of atherosclerotic area		G1	G2	t. test	*p*. value
RT	Mean+SD	1.35±0.40	1.11±0.34	2.635	0.048*
LT	Mean+SD	1.27±0.30	1.01±0.25	3.147	0.042*
t. test		1.190	1.152		
p. value		0.227	0.323		
Transverse diameter of atherosclerotic area		G1	G2	t. test	*p*. value
RT	Mean+SD	1.24±1.18	1.05±0.27	2.358	0.046*

LT	Mean+SD	1.20±0.26	1.0±0.23	2.110	0.038*
t. test		0.639	0.953		
p. value		0.635	0.241		

Table (4): demographic, clinical and laboratory findings in atherosclerotic and non-atherosclerotic patients

parameter	Atherosclerotic group	Non atherosclerotic group	t. test	*P* value
SGOT (u/l)	32.25±8.69	26.14±5.36	0.324	0.429
SGPT (u/l)	30.24±7.63	24.19±13.2	0.620	0.096
S.ALB (g/dl)	4.25±1.25	3.26±2.24	0.284	0.178
HB% (gm/dl)	10.24±0.96	8.63±2.69	0.428	0.658
R.B.Cs (×106/cc)	4.21±0.96	2.41±0.85	0.252	0.099
PLATELETS	175214.2±3695.2	150230±7453.2	0.069	0.521
T.L.C	6152±1583.2	5471.2±369.2	0.258	0.878
PHOPHORUS (mg/dl)	5.69±1.24	4.65±0.36	0.536	0.414
S.CACIUM(mg/dl)	0.88±0.18	0.74±0.62	0.447	0.417
PTH (pg/ml)	452.6±69.3	258.3±19.5	3.626	0.028*
PT (seconds)	16.24±2.36	10.35±8.36	0.365	0.634
PT. CONC (%)	84.16±13.52	82.36±18.63	0.325	0.563
INR	1.34±0.25	1.30±0.24	0.325	0.471
PTT	41.36±6.35	39.51±3.74	0.536	0.414
F.B.S (mg/dl)	83.41±6.35	80.99±7.85	0.447	0.417
Systolic B.P (mm.hg)	120.25±3.63	116.35±7.52	0.365	0.634
Diastolic B.P (mm.hg)	85.36±7.52	83.15±6.52	0.325	0.563
BMI	24.41±3.25	23.41±2.99	0.325	0.471
Age (years)	44.36±3.25	41.62±4.95	0.530	0.258

Table (5): Comparison of lipid profile betweenatherosclerotic and non-atherosclerotic patients

parameter	Atherosclerotic group	Non atherosclerotic group	t. test	*p*. value
CHOL	151.6±36.25	134.52±26.52	5.326	0.020*
TGS	147.62±33.25	142.95±28.63	0.635	0.241
LDL	88.42±15.28	62.35±17.5	4.968	0.018*
HDL	37.52±63.54	39.52±18.96	0.856	0.224

4. Discussion

In the present work, there was no significant difference between studied groups as regard age, BMI, systolic and diastolic BP, pre and post dialytic blood urea, serum creatinine and BUN.

The present study found significantly higher plasma PTH levels in HCV infected patients compared with those who were HCV negative. **Azza *et al.,*** 2015, found in a previous work that serum level of PTH was higher in patients with hepatitis C virus infection than controls which is consistent with our data.

This association of hepatitis C virus infection and high serum level of PTH could be explained on bases of reduced specific vitamin D receptors (VDRs) in liver cells in patients with chronic hepatitis C virus infection **(Barchetta *et al.,* 2012)**. This might compromise the negative effect of chronic kidney disease on activation of vitamin D. Other research works carried-out by **Yenice *et al.,* 2006 and Miroliaee *et al.,* 2010**, revealed normal or low PTH levels in HCV infection, but in these research works patients had no chronic kidney disease and we should consider the high prevalence of vitamin D deficiency in Egypt.

Our work showed that serum levels of total cholesterol and LDL-Ch. were significantly higher in patients with hepatitis C virus infection than those with no hepatitis C virus infection, but there was no significant difference in serum levels of HDL-Ch and triglycerides between both group.

Most of previous works do not support our results. **Ehab, 2010,** demonstrated that patients with chronic HCV infection had significant lower serum levels of LDL-Ch, total cholesterol, and triglycerides than normal persons with comparable age, sex and BMI. Similarly; **Camila *et al.,* 2012,** found that the serum levels of HDL-Ch, very low-density lipoprotein (VLDL) and triglycerides of chronic hepatitis C patients were lower than those of the control group.

Low lipid profile in patients with chronic hepatitis C virus infection as shown in previous studies can be justified by the findings of other research works which revealed a HCV-specific effect

on lipids, resulting either from differential effects on liver function or from a direct interaction with lipid metabolism **(Fabris *et al.*, 1997)**. Some studies suggest that HCV core protein decreases the activity of the microsomal triglycerides transfer protein, leading to decreased hepatic VLDL assembly and secretion **(Thomssen *et al.*, 1992; Wunschmann et al., 2000; Perlemuter *et al.*, 2002).** In addition, there is evidence that HCV particles associate with LDL and VLDL particles in the plasma and utilize the LDL receptors for cell binding, possibly leading to increased lipid uptake by cells **(Thomssen *et al.*, 1992; Wunschmann *et al.*, 2000).**

Ooi *et al.*, 2005, studied the dyslipidemia in various liver diseases, such as chronic hepatitis, hepatic cirrhosis, hepatocellular carcinoma and metastatic hepatic diseases. They discovered anomalies in lipid metabolism in several hepatic diseases, for example, in chronic hepatitis, cirrhosis and hepatocellular carcinoma, they found that the LDL-Ch fraction had increased. This result is consistent with ours and with **Camila *et al.*, 2012**, who reported that serum level of LDL-Ch in HCV positive patients was higher than those who were HCV negative patients. Also, **Camila *et al.*, 2012**, found that serum level of apolipoprotein B was higher in HCV positive patients. **Kathleen *et al.*, 2009,** demonstrated that differences of serum levels of HDL-Ch and triglyceride were not statistically significant between the HCV group and uninfected controls which support our findings. The finding of higher LDL-Ch in HCV positive patients has no clear explanation, but genetic predisposition and HCV genotype may play a role.

The present study revealed a significantly higher longitudinal and transverse diameters of atherosclerosis in right and left common carotid arteries in HCV positive patients than those with no hepatitis C virus infection. Our result indicates the higher risk of atherosclerosis in patients with ESRD on hemodialysis with HCV infection.

This finding is in agreement with **Lee *et al.*, 2010**, as they demonstrated that the hazard ratio of cerebrovascular death was 2.18 (95% CI, 1.50–3.16) for HCV-seropositive subjects after adjustment of conventional risk factors. In their study, no specific HCV genotype was found to be more strongly (or weakly) associated with cerebrovascular death. In addition, by comparing individuals with stroke and age- and gender-matched subjects, **Adinolfi *et al.*, 2012,** reported that the prevalence of HCV-antibody positivity was significantly higher among patients with stroke (26.8%) than among control patients (6.6%), with an odds ratio of 2.04 after multivariate adjustment. They also analyzed the prevalence of ischemic heart events among the study participants, and found that such events were significantly more prevalent among the HCV-positive patients (22%) than among the HCV-negative subjects (13%). These findings suggested that HCV infection may be associated with a higher prevalence of atherosclerotic disease.

Also, **Petta *et al.*, 2012,** reported that HCV infected patients had a significantly higher prevalence of atherosclerosis than matched control subjects (41.9% vs 22.9%, respectively). In an Egyptian study, Mostafa ***et al.*,** 2010**,** demonstrated similar results, as they stated that HCV infected patients showed a higher risk of atherosclerosis following adjustment for known cardiovascular risk factors.

On the other hand**, Kiechl *et al.*, 2001,** examined five-year changes in carotid atherosclerosis by high-resolution duplex scanning, and found a strong association between the development of new atherosclerotic lesions and respiratory, urinary, and other types of chronic infectious illness, including infections of *C. pneumoniae*; however, HCV seropositivity was found to be unrelated to early stage atherogenesis. In a population-based study, **Miyajima *et al.*, 2013,** demonstrated, in reverse, that patients with chronic HCV infection had significantly decreased carotid intima-media thickness as compared with non-infected subjects.

The precise pathogenic mechanisms connecting HCV infection, chronic liver disease, and atherogenesis are not completely understood. However, several factors might mediate the link, between HCV infection and atherogenesis. These include disrupted iron homeostasis, increased oxidative stress **(Yadav *et al.*, 2002),** induction of hepatic steatosis leading to aggravated insulin resistance and other related metabolic abnormalities **(Adinolfi *et al.*, 2001),** activation of immunological and/or inflammatory processes and associated cytokine imbalance (**Jacobson and Neuman, 2001; Oliveira *et al.*, 2013**) and in situ viral replications **(Boddi *et al.*, 2007).** In our study, the higher serum levels of PTH and LDL-Ch in patients with HCV infection can add to the explanation of higher risk of carotid atherosclerosis in this group of patients. As it is hypothesized that disturbance in the endocrine Ca - PTH- vitamin D axis seems to play a role in the pathogenesis of osteo-metabolic disturbances (**Azza *et al.*, 2015).**

Epidemiological and clinical studies have consistently demonstrated that an elevated LDL- Ch concentration in the plasma is associated with an increased risk of coronary artery disease (CAD) **(Grundy, 2002; Grundy *et al.*, 2004)**. Increased LDL-Ch concentration is a well-established risk factor for CAD, which suggests that the risk of HCV patients developing vascular complications is higher.

In conclusion:

We conclude that HCV infection in hemodialysis patients increases the risk of atherosclerosis as proved by carotid duplex. Therefore, we recommend aggressive management of other cardiovascular risk factors in these patients for prevention of cardiovascular events.

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References:

1. Adinolfi, L. E.; Gambardella, M.; Andreana, A.; Tripodi, M. F.; Utili, R. and Ruggiero, G., (2001): Steatosis accelerates the progression of liver damage of chronic hepatitis C patients and correlates with specific HCV genotype and visceral obesity. Hepatology; 33:1358–64.
2. Afifi, A., (2008): Annual reports of the Egyptian renal registry; 1996-2008, http://www.esnonline.net.
3. Alter, M. J., (2007). Epidemiology of hepatitis C virus infection. World J Gastroenterol;13:2436-2441.
4. Ansar, M. M. and Kooloobandi, A., (2002): Prevalence of hepatitis C virus infection in thalassemia and haemodialysis patients in north Iran-Rasht. Journal of Viral Hepatology;9:390-392.
5. Aslam, F.; Alam, M. and Lakkis. N. M., (2010): Hepatitis C and carotid atherosclerosis: a retrospective analysis. Atherosclerosis; 209: 340-3.
6. Azza, A, E. and Madleen, A. A., *et al.* (2015): Vitamin D status and viral response to therapy in hepatitis C infected children. WJG 2015 28; 21(4): 1284-1291.
7. BALLANTI, P.; SILVESTRINI, G. and PISANÒ, S., *et al.* (2011): Medial artery calcification of uremic patients: a histological, histochemical and ultra structural study. Nephrology Dial Transplant; 26: 349-357.
8. Barchetta, I.; Carotti, S.; Labbadia, G. and Gentilucci, U, V., *et al*. (2012): Liver vitamin D receptor, CYP2R1, and CYP27A1 expression: relationship with liver histology and vitamin D3 levels in patients with nonalcoholic steatohepatitis or hepatitis C virus. Hepatology; 56: 2180-2187.
9. Boddi, M.; Abbate, R. and Chellini, B., *et al.* (2007): HCV infection facilitates asymptomatic carotid atherosclerosis: preliminary report of HCV RNA localization in human carotid plaques. Dig Liver Dis; 39(suppl 1):S55–60.
10. Coll, B.; Betriu, A. and Martinez-Alonso, M., *et al.* (2010): Cardiovascular risk factors underestimate atherosclerotic burden in chronic kidney disease: usefulness of non-invasive tests in cardiovascular assessment. Nephrol Dial Transplant; 25: 3017-3025.
11. Collins, A. J., (2003): Cardiovascular mortality in end-stage renal disease. Am J Med Sci; 325: 163-167.
12. Corey, E. K.; Erin, E. k.; Munroe, C. C.; Barlow, L. L.; Zheng, H. H.; Raymond. T. and Chung, T. M., (2009): Hepatitis C Virus Infection and Its Clearance Alter Circulating Lipids: Implications for Long Term Follow-up. Hepatology; 50(4): 1030–1037.
13. Ehab, H. N., (2010): Lipid profile among chronic hepatitis C Egyptian patients and its levels pre and post treatment. Nature and Science; 8(7): 83-89.
14. Fabris, C.; Federico, E.; Soardo, G.; Falleti, E. and Pirisi, M., (1997): Blood lipids of patients with chronic hepatitis: differences related to viral etiology. Clin Chim Acta;261(2):159-65.
15. Grundy, S. M., (2002): Low-density lipoprotein, non-high-density lipoprotein, and apolipoprotein B as targets of lipid-lowering therapy. Circulation; 106(20):2526-9.
16. Grundy, S. M.; Cleeman, J. I. and Merz, C. N., *et al.* (2004): Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. Circulation; 110(2):227-39.
17. Jacobson, P. M. and Neuman, M. G., (2001): Immunopathogenesis of hepatitis C viral infection: Th1/Th2 responses and the role of cytokines. Clin Biochem; 34:167–71.
18. Kiechl, S.; Egger, G. and Mayr, M., *et al.* (2001): Chronic infections and the risk of carotid atherosclerosis: prospective results from a large population study. Circulation; 103:1064–70.
19. Lee, M. H.; Yang, H. I. and Wang, C.H., *et al.* (2010): Hepatitis C virus infection and increased risk of cerebrovascular disease. Stroke; 41:2894–900.
20. Miroliaee, A; Nasiri-Toosi, M. and Khalilzadeh, O., *et al*. (2010): Disturbances of parathyroid hormonevitamin D axis in non-cholestatic chronic liver disease: a cross sectional study. *Hepatol Int*; 4: 634-640.
21. Miyajima, I.; Kawaguchi, T. and Fukami, A., *et al.* (2013): Chronic HCV infection was associated with severe insulin resistance and mild atherosclerosis: a population-based study in

an HCV hyperendemic area. J Gastroenterol; 48:93–100.
22. Mohamoud, Y.; Mumtaz, G.; Riome, S.; Miller, D. and Abu-Raddad, L., 2013: The epidemiology of hepatitis C virus in Egypt: a systematic review and data synthesis. BMC Infect Dis; 13:288.
23. Mostafa, A.; Mohamed, M. K. and Saeed, M., *et al.* (2010): Hepatitis C infection and clearance: impact on atherosclerosis and cardiometabolic risk factors. Gut; 59: 1135-1140.
24. Oliveira, C. P.; Kappel, C. R. and Siqueira, E. R., *et al.* (2013): Effects of hepatitis C virus on cardiovascular risk in infected patients: a comparative study. Int J Cardiol;164:221–6.
25. Ooi, K.; Shiraki, K.; Sakurai, Y.; Morishita, Y. and Nobori, T., (2005): Clinical significance of abnormal lipoprotein patterns in liver diseases. Int J Mol Med; 15(4):655-60.
26. Perlemuter, G.; Sabile, A. and Letteron, P., *et al. (*2002): Hepatitis C virus core protein inhibits microsomal triglycerides transfer protein activity and very low density lipoprotein secretion: a model of viral-related steatosis. Faseb J;16(2):185-94.
27. Petta, S.; Torres, D. and Fazio, G., *et al.* (2012): Carotid atherosclerosis and chronic hepatitis C: a prospective study of risk associations. Hepatology; 55: 1317-1323.
28. Roman, M. J.; Naqvi, T. Z. and Gardin, J. M., *et al.* (2006): American Society of Echocardiography Report. Clinical application of noninvasive vascular ultrasound in cardiovascular risk stratification: a report from the American Society of Echocardiography and the Society for Vascular Medicine and Biology. Vasc Med; 11: 201–211.
29. Thomssen, R.; Bonk, S.; Propfe, C.; Heermann, K. H.; Kochel, H, G. and Uy, A., (1992): Association of hepatitis C virus in human sera with beta-lipoprotein. Med Microbiol Immunol; 181(5):293-300.
30. Wunschmann, S.; Medh, J. D.; Klinzmann, D.; Schmidt, W. N. and Stapleton, J. T., (2000): Characterization of hepatitis C virus (HCV) and HCV E2 interactions with CD81 and the low-density lipoprotein receptor. J Virol; 74(21):10055-62.
31. Yadav, D.; Hertan, H. I.; Schweitzer, P.; Norkus, E. P. and Pitchumoni, C. S.,(2002); Serum and liver micronutrient antioxidants and serum oxidative stress in patients with chronic hepatitis C. Am J Gastroenterol; 97:2634–9.
32. Yenice, N.; Gümrah, M. and Mehtap, O., *et al.* (2006): Assessment of bone metabolism and mineral density in chronic viral hepatitis. Turk J Gastroenterol; 17: 260-266.

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