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RESEARCH ARTICLE

CHRONIC HEPATITIS B AND C VIRUSES INFECTION AS A RISK FOR ATHEROSCLEROSIS IN ZAGAZIG UNIVERISTY HOSPITALS

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Abstract

Background & Aims: To compare carotid intima-media thickness (IMT) – an index of early atherosclerosis – among patients with chronic hepatitis B (HBV), chronic hepatitis C (HCV) and control subjects.

Patients and Methods: We studied 20 patients with HCV, 20 patients with HBV, and 20 healthy controls who were comparable for age and sex. Common carotid IMT was measured with ultrasonography in all participants by a single operator blinded to subjects' characteristics.

Results: Carotid IMT measurements were markedly different among the groups; the lowest values were in controls, and, intermediate in patients with HBV and HCV (0. 0.7 ± 0.1 vs. 1 ± 0.2vs. 1.1 ± 0.2 respectively; $p < 0.001$). The marked differences in carotid IMT that were observed among the groups were little affected by adjustment for age, sex, body mass index, smoking, LDL cholesterol .Concordantly, HBV and HCV predicted carotid IMT independent of potential confounders.

Conclusions: These data suggest that HCV and HBVespecially non cirrhotic patients are strongly associated with early atherosclerosis independent of classical risk factors.

INTRODUCTION

Hepatitis C virus (HCV) infection is a major social, medical, and economic problem. It has been estimated that global prevalence around 3%. In Egypt ,the prevalence of the two major biomarkers of HCV-the anti HCV antibodies and HCV RNA seropositivity is estimated at 14.7% and 9.8% respectively,in the general population and this has largely been attributed to the parenteral anti -schistosomal therapy campaigns that took place from the 1950s through the 1980s **, (1), (2)**

he prevalence of HBV varies between 2% in developed countries where the prevalence is low to about 8% in developing countries where the infection is endemic with sex,age and socio economic status as important risk factors for infection.Countries are classified as having low endemic rates(<2%),intermediate endemic rates (2-8%),or high endemic rates(≥8%) positive for HBSAg.The prevalence of HBV in Egypt is of intermediate endemicity**(2-8%), (3), (** 4)

Several possible mechanisms may exist to explain the relationship between HBV infection and atherosclerosis. First, HBV may colonize in the vascular tissues, leading to vascular damage. Second, HBV infection

occasionally is associated with vasculitis. Third, chronic HBV infection may be associated with increased levels of oxidative stress, which may accelerate atherogenesis. Finally, chronic HBV infection may stimulate inflammatory and immune-mediated responses **(**5)

Ross et al [6]have been reported in hypothesis called response to injury and suggested the involvement of the endothelium in the development of atherosclerosis and chronic heart disease. They indicate that the inflammatory events have a pivotal role in the etiopathology and evolution of sclerotic lesions.There are many risk factors such as smoking, diabetes mellitus, hypertension and dyslipedemia may provoke endothelial injury and this damage may trigger the inflammatory response [6]However, many patients develop atherosclerosis in the absence of the established risk factors**,** [7], This observation has stimulated efforts to find alternative nontradiational determinants that may be involved in the initiation and progression of atherosclerotic process. Infectious agents including hepatitis virus (B and C) may have a role in these events [8] However, a sure pathogenic link between infection particularly with hepatitis B and C virus and atherosclerosis remains under debate **[9]**

Methods

This study had been carried out in Internal Medicine, and Diagnostic Radiology Departments, Faculty of Medicine, Zagazig University **(from June 2013 to June 2015).** The study was done on 60 subjects; they were classified into 3 groups:

Group I:

It included twenty apparently healthy subjects. They had normal clinical examination, liver enzymes, biochemical, hematological investigations negative ultrasonographic pathological findings,…..etc. Eight males and twelve females their ages ranged from 45-50 with mean ± SD 47.6 ± 1.7 years.

Group II:

It included twenty patients with chronic hepatitis C virus (HCV)infection . Diagnosis was based on seropositivity of anti HCV antibody .Positive cases were confirmed by(HCV-PCR). Eight males, and twelve females their ages ranged from 45-50 with mean ± SD **46.6 ± 2.7** years.

GroupIII:

It included twenty patients with chronic hepatitis B virus (HBV) infection . Diagnosis was based on seropositivity of HBsAG .Positive cases were confirmed by(HBV PCR). Eight males and twelve females their ages ranged from 40-50 with mean ± SD **45.6 ± 3.9** years.

Inclusion Criteria

1. Age more than 18 years old.

2. Both sexes.

3. Any hepatic infected with viral hepatitis B and C cirrhotic and non cirrhotic.

Exclusion criteria:

1- Age less than 18 years old.
2- Patients refuse to enter the study.
3- Pregnant patients.
4- Missed patient's data.
5- Patients infected with hepatitis viruses other than B and C and also patients with chronic liver diseases eg.bilharziasis
6- Other risk factors of atherosclerosis as Hypertension, Diabetes, smoking and alcoholic intake.

8-Patients on lipid lowering medications

Type of the study: Comparative Cross-sectional study.

Administrative design:

Approval of internal medicine department of Zagazig faculty of medicine, approval of IRB & ethical committee in Zagazig faculty of medicine were all taken.

Ethical clearance.

Written informed consent from the patients if possible or from their relatives to participate in the study.

All participates of the study were subjected to the following:

(1) Thorough history taking and detailed clinical examination according to included work sheet with special stress on, age, gender, etiology of liver disease , risk factors for atherosclerosis, duration, source of liver infections, and types of medications received . History of hypertension, diabetes, and cardiovascular complications including angina, CVS, and myocardial infarction

.Complete clinical examination

(2) Routine investigations include:

All investigations were done according to methods applied to the clinical pathology and laboratories of Zagazig university hospital and include;

- Complete blood cell count (CBC), ***(by automated blood counter*** **cell Dyne 1700**)
- Liver function tests as Serum albumin, total bilirubin, SGOT, and SGPT measured by automated Autoanalyser COBAS 501 C.
- Serology of HCV and HBV(PCR) by ELISA
- Anti HCV antibody
- HBsAg
- Bleeding profile (PT and INR) by **automated sysmex CA 1500..**

(3) Abdominal ultrasonography

(4) Special investigations including:

- Lipid profile as total cholesterol, LDL, HDL, and serum Triglyceride by **automated Autoanalyser COBAS 501 C..**
- Measurement of carotid intima-media thickness **(10).**

Measurement of common carotid intima-media thickness

A single operator blinded to subjects' characteristics measured common carotid IMT using B-mode ultrasonography 7.5 MHz probe. IMT measurements were made bilaterally in the 1-cm segment proximal to the dilatation of the carotid bulb. For each subject, three maximum values of carotid IMT on both sides were measured, on the anterior, lateral and posterior projection of the near and far wall. All readings were then averaged.

Repeated measurements on the same subjects gave coefficients of variation below 9% , ***Targher G***., **et al** (**11**) Previous studies have shown that normal IMT values vary according to age and atherosclerosis-related risk factors, ranging from 0.60-0.75 mm (30-49 years) to 0.79-0.86 mm (50-79 years), **.**(12) **.**A carotid plaque was defined as a focal thickening of ≥1.3 mm at the level of common carotid artery **(10).**

Statistical Methods

Data collected throughout history,basic clinical examination,laboratory investigations and outcomes measures coded ,entered and analyzed using Microsoft Excel software .

Data were then imported into Statistical Package for the Social Science(**SPSS version 20.0**) (**Statistical Package for the Social Science)** software for analysis

* Mean ± standard deviation with Median and range when appropriate described quantitive data.Numbers with percentages described qualtitive data.chi square test (X2) and fisher exact was used to compare proportions* ANOVA, LSD, independent t test and are used to compare different parametric parameters.

* Correlations by Pearson Correlations

* P value is considered significant at ≤ 0.05 level, highly significant at ≤ 0.001 and non-significant at > 0.05.

RESULTS

Table (1): Showed a statistically high significant difference as regard mean value ± SD of PLT.count ***(x103/mm3)***, AST (U/L) ,ALT (U/L) ,GGT (U/L), HDL (mg/dl) (P≤0.001) among the different groups of the study

using ANOVA test .A significant difference was found as regard mean value ± SD of WBCs ***(****cells/mm^3****)***, HB (g/dl) ,PT (Sec**)**, INR, S.ALBUMIN (mg/dl), T.CHOLESTEROL (mg/dl) and LDL (mg/dl) . (P≤0.05).No significance difference was found as regard mean value± SD o fage (years),sex, T.BILIRUBIN (mg/dl) and TGs (mg/dl) (P 0.298)

Table (2): demonstrated a statistically significant difference between

HCV and HBV patients in comparison to control subjects as regard total cholesterol. While no significance difference between HCV and HBV patients .

Table(3): demonstrated a statistically high significant difference betweenHCV and HBV patients in comparison to control subjects as regard HDL.While

No significance difference between HCV and HBV patients

Table (4): showed a statistically high significant difference between HCV and HBV patients in comparison to control subjects as regard LDL.While
No significance between HCV and HBV patients.

Tables(5&6): demonstrateda statistically highly significant difference of CIMT(mm) in HCV patients and HBV patients as compared to control group but no significant difference between HCV patients and HBV patients (P<0.001).

Table(7): demonstrated a statistically highly significant increase in the mean values ± SD of carotid intima media thickness (mm) in HCV Non-cirrhotic patients in comparison to HCV cirrhotic patients(P<0.001).

Table(8): showed a statistically highly significant increase in the mean values ±SD of carotid intima media thickness (mm) in HBV Non-cirrhotic patients in comparison to HBV cirrhotic patients(P<0.001).

Table(9): demonstratd a statistically highly significant increase in the mean values± SD of CIMT(mm) in Non-cirrhotic patients in comparison to cirrhotic patients(P<0.001).

Table (10): showed the prevalence of significant difference of carotid intima media thickness (CIMT) in the different groups of the study . CIMT ≥1.3 mm was found in 0 % ofcontrol group, 52.9% of HCV patients and 47.1% of HBV patients with highly significant difference between them.

Table (11): showed no significant correlations between CIMT and other studied parameters in control group p≥ 0.05.

In HCV patients; there were highly significant positive correlations between CIMT(mm) and WBCs *(cells/mm^3)*, PLT *(x103/mm3)* ,S.ALBUMIN (mg/dl), ALT (U/L), GGT (U/L), T.CHOLESTEROL (mg/dl), TGs (mg/dl) and LDL (mg/dl)**(p <0.001**) .Also there were significant positive correlations between CIMT(mm) and HB (g/dl)**(p <0.05) .** There were highly significant negative correlations between CIMT(mm) and PT (**Sec)**, INR **(p <0.001**). No significant correlations as regarad AGE (years), AST (U/L) ,T.BILIRUBIN (mg/dl) and HDL (mg/dl) were found(p> 0.05).

In HBV patients; there were highly significant positive correlations between CIMT(mm) and PLT.count *(x103/mm3)* , GGT (U/L), T.CHOLESTEROL (mg/dl), and LDL (mg/dl) **(p ≤0.001**).Also there were significant positive correlations between CIMT(mm) and HB (g/dl), S.ALBUMIN (mg/dl) and TGs (mg/dl) **(p ≤0.05)** .Also there was significant negative correlations between CIMT (mm) and PT (**Sec)**, INR and T.BILIRUBIN (mg/dl) **(p ≤0.05)**. There were no significant correlations as regarad AGE (years), ALT (U/L), WBCs *(cells/mm^3)*and HDL (mg/dl), and AST (U/L) (p> 0.05).

Table(11):showed no significant correlations between CIMT and PCR between HCV and HBV patients.

Figure (1): showed Mean values of Lipid profile in different study groups
Figure (2): demonstrated The prevalence of carotid intima media thickness (CIMT <1.3 and ≥1.3 mm) in the different groups of the study

Table(1) Demographic and laboratory data of different study groups

Variable		Control	HCV	HBV	Value	P
Male	No. (%)	12 (60%)	12 (60%)	12 (60%)	0.000	1.000
Female		8 (40%)	8 (40%)	8 (40%)		
AGE (years)	Mean ± SD	47.6 ± 1.7	46.6 ± 2.7	45.6 ± 3.9	2.40	.099
WBCs ***(cells/mm^3)***	Mean ± SD	7.1 ± 2.3	4.9 ± 2.5	6.3 ± 2.8	3.62	.033*
HB (g/dl)	Mean ± SD	11.3 ± 1	9.9 ± 1.1	10.4 ± 1.5	6.81	.002*
PLT ***(x103/mm3)***	Mean ± SD	294.8 ± 90.9	163.7 ± 91.4	174.2 ± 93	12.61	.000**
PT (**Sec)**	Mean ± SD	12 ± 0.7	14.6 ± 3.3	15 ± 3.5	6.90	.002*
INR	Mean ± SD	0.9 ± 0.1	1.4 ± 0.7	1.5 ± 0.7	6.98	.002*
S.ALBUMIN (mg/dl)	Mean ± SD	4.1 ± 0.5	3.4 ± 1.2	3.2 ± 1	5.22	.008*
T.BILIRUBIN (mg/dl)	Mean ± SD	0.9 ± 0.1	2 ± 3	2.7 ± 2.6	2.96	.060
AST (U/L)	Mean ± SD	16.8 ± 3.2	76.7 ± 16.1	50.8 ± 28.5	50.08	.000**
ALT (U/L)	Mean ± SD	16 ± 3.5	81.2 ± 29.1	60 ± 35.2	31.62	.000**
GGT (U/L)	Mean ± SD	14.6 ± 3.6	53.8 ± 22	45.1 ± 20.1	11.47	.000**
T.CHOLESTEROL (mg/dl)	Mean ± SD	108.3 ± 14.4	149.8 ± 67.3	154.9 ± 65.1	4.36	.017*
TGs (mg/dl)	Mean ± SD	83.7 ± 13.2	90.2 ± 40	104.3 ± 60.1	1.24	.298
HDL (mg/dl)	Mean ± SD	64.6 ± 6.5	41.1 ± 12.3	37.6±7.5	51.93	.000**
LDL (mg/dl)	Mean ± SD	66 ± 14.6	95.3 ± 51.6	96.9±49.3	3.43	.039*

*** Significant Difference p ≤ 0.05 ** Highly significant Difference p ≤0.001**

Table (2): Total Cholesterol (mg/dl) among different study groups (LSD).

	Control	HBV
HCV	<0.05	NS
HBV	<0.01	

Table (3): HDL(mg/dl) among different study groups(LSD).

	Control	HBV
HCV	<0.001	NS
HBV	<0.001	

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Table (4): LDL(mg/dl) among different study groups(LSD).

	Control	HBV
HCV	<0.05	NS
HBV	<0.05	

Figure (1): Mean values of Lipid profile in different studied groups

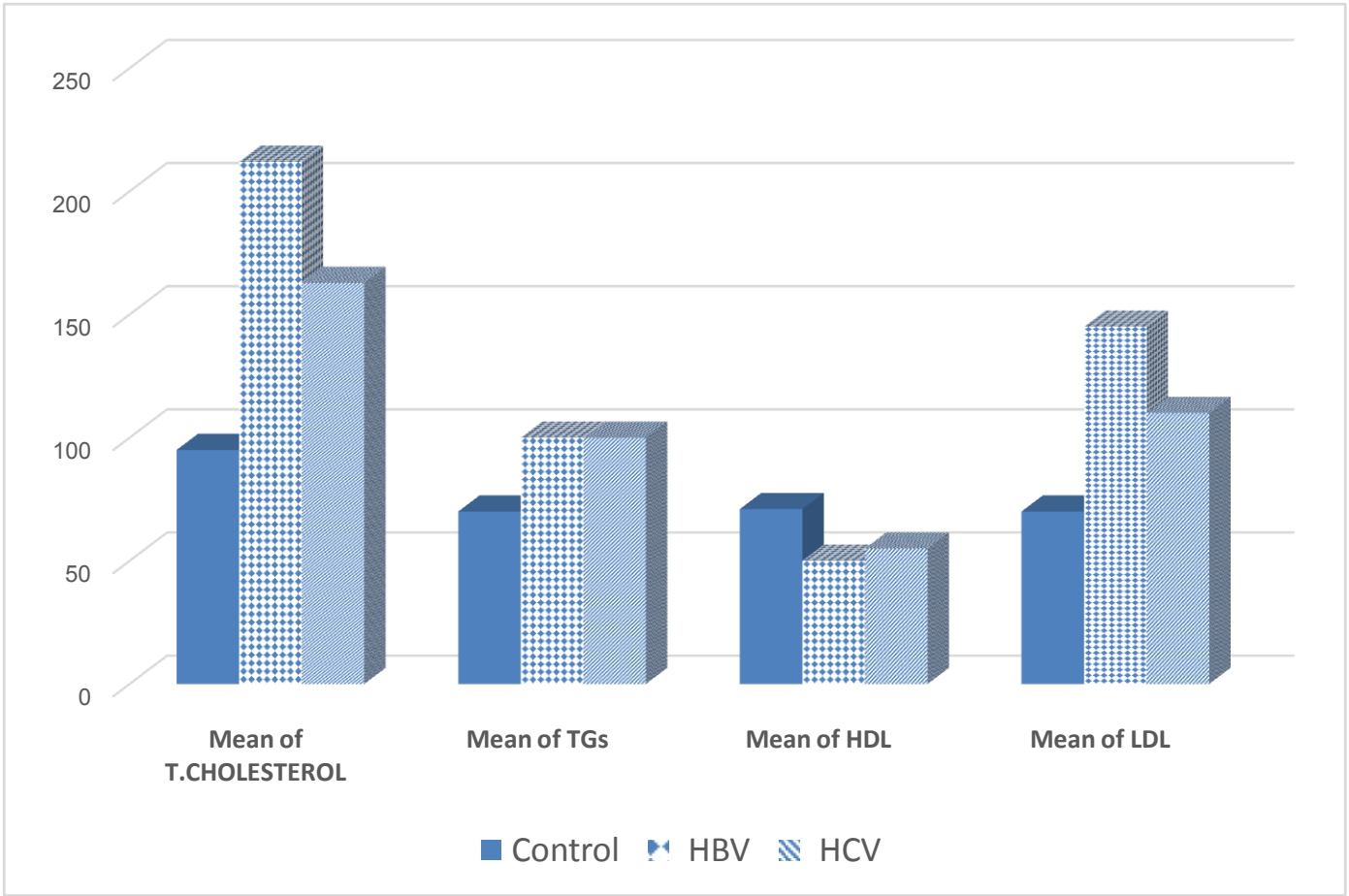


Table (5): Comparisons between mean values ± SD of Carotid intima media thickness (CIMT) among different studied groups (ANOVA)

	Control Mean ± SD	**HCV** Mean ± SD	**HBV** Mean ± SD	**Value**	**P**
CIMT (mm)	0.7 ± 0.1	1.1 ± 0.2	1 ± 0.2	23.89	.000**

Table (6): CIMT (mm) among the different study groups (LSD).

	Control	***HBV***
HCV	<0.001	NS
HBV	<0.001	

Table (7): Comparisons between mean values ± SD of carotid intima media thickness (mm) between cirrhotic and non-cirrhotic HCV patients.

	HCV Non-cirrhotic patients	HCV cirrhotic patients	value	p
	Mean ± SD	Mean ± SD		
CIMT	1.3 ± 0.1	0.9 ± 0.1	10.24	.000**

Table (8): Comparisons between mean values ± SD of CIMT between cirrhotic and non-cirrhotic HBV patients.

	HBV Non-cirrhotic patients	HBV cirrhotic patients	value	p
	Mean ± SD	Mean ± SD		
CIMT	1.2 ± 0.2	0.9 ± 0.1	4.832	.000**

Table (9): Comparisons between mean values ± SD of carotid intima media thickness between cirrhotic and non-cirrhotic patients.

	Non-Cirrhotic CLD (HBV & HCV)	Cirrhotic CLD (HBV & HCV)	value	p
	Mean ± SD	Mean ± SD		

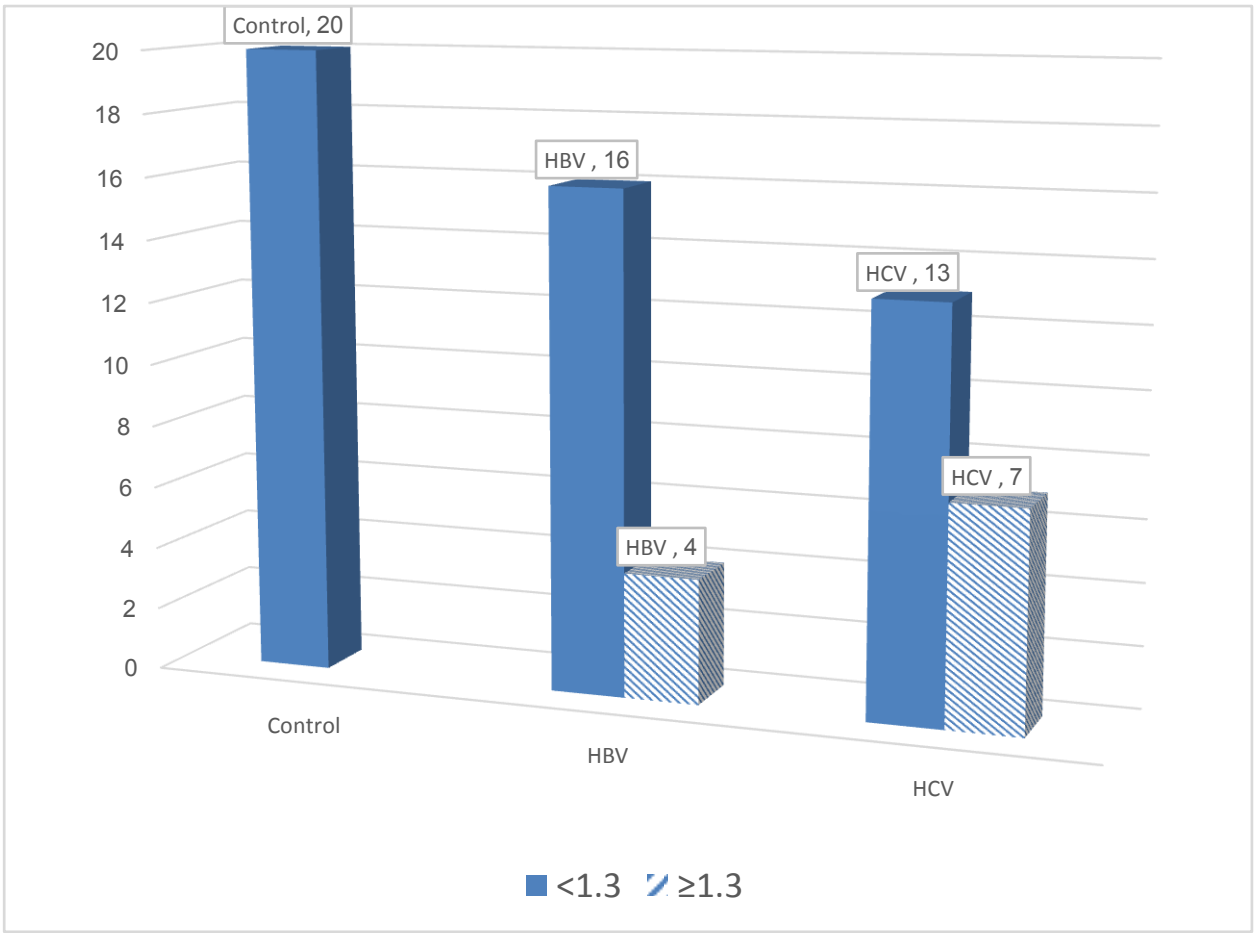
CIMT	1.2 ± 0.1	0.9 ± 0.1	-9.255	.000**

Table (10): The prevalence of carotid intima media thickness (CIMT <1.3 and ≥1.3 mm) in the different studied groups.

CIMT		Control	HCV	HBV	Value	Sig.
<1.3 mm	N	20	49	16	8.237	.016*
	%	100.0%	65.0%	80.0%		
≥1.3 mm	N	0	7	4		
	%	0.0%	35.0%	20.0%		

CIMT≥1.3 mm means carotid plaque CIMT<1.3 mm no carotid plaques **(PETTA et al,2012).**

Figure (2): The prevalence of carotid intima media thickness (CIMT <1.3 and ≥1.3 mm) in the different groups of the study



	Control		HCV		HBV	
	r	P-value	**r**	P-value	**r**	**P-value**
AGE (years)	-.439	.053	.268	.254	.155	.514
WBCs *(cells/mm^3)*	-.099	.679	.726	.000**	.417	.067
HB (g/dl)	-.068	.777	.484	.031*	.526	.017*
PLT *(x103/mm3)*	-.100	.675	.727	.000**	.730	.000**
PT (Sec)	.107	.652	-.799	.000**	-.636	.003*
INR	.134	.572	-.773	.000**	-.591	.006*
S.ALBUMIN (mg/dl)	-.121	.613	.900	.000**	.646	.003*
T.BILIRUBIN (mg/dl)	-.312	.180	-.413	.071	-.586	.007*
AST (U/L)	-.425	.061	.068	.775	-.007	.977
ALT (U/L)	-.214	.365	.893	.000**	.083	.728
GGT (U/L)	-.170	.473	.777	.000**	.822	.000**
T.CHOLESTEROL (mg/dl)	-.079	.742	.877	.000**	.811	.000**
TGs (mg/dl)	.242	.303	.884	.000**	.608	.004*

HDL (mg/dl)	.103	.667	-.272	.246	.215	.362
LDL (mg/dl)	-.174	.463	.901	.000**	.812	.000**

Table (11): *Correlation between (CIMT) and other studied parameters*

*** Significant Difference p ≤ 0.05 ** Highly significant Difference p ≤0.001**

Table (12): Correlation between (CIMT) and PCR values in HCV and HBV

	HCV		**HBV**	
	r	Sig.	r	Sig.
CIMT	-.064	.788	-.319	.170

Discussion

Hepatitis C virus (HCV) infection is a major social, medical, and economic problem. It has been estimated that global prevalence around 3%. In Egypt ,the prevalence of the two major biomarkers of HCV-the anti HCV antibodies and HCV RNA seropositivity is estimated at 14.7% and 9.8% respectively,in the general population and this has largely been attributed to the parenteral anti -schistosomal therapy campaigns that took place from the 1950s through the 1980s **, (1), (2)**

The prevalence of HBV varies between 2% in developed countries where the prevalence is increased to about 8% in developing countries where the infection is endemic with sex,age and socio economic status as important risk factors for infection.Countries are classified as having low endemic rates(<2%),intermediate endemic rates (2-8%),or high endemic rates(≥8%) positive for HBSAg.The prevalence of HBV in Egypt is of intermediate endemicity**(2-8%), (3), (4).**

There are many risk factors such as smoking, diabetes mellitus, hypertension and dyslipedemia may provoke endothelial injury and this damage may trigger the inflammatory response **(6).** However, many patients develop atherosclerosis in the absence of the established risk factors **(7).** This observation has stimulated efforts to find alternative nontradiational determinants that may be involved in the initiation and progression of atherosclerotic process. Infectious agents including hepatitis virus (B and C) may have a role in these events (8). However, a sure pathogenic link between infection particularly with hepatitis B and C virus and atherosclerosis remains under debate **(9).**

Ross et al (6) suggested the involvement of endothelium in the development of atherosclerosis and chronic heart disease. They indicate that the inflammatory events have a pivotal role in the etiopathology and evolution of sclerotic lesions.

Interactions between chronic hepatitis C virus (HCV) infection and lipid metabolism have been described in some studies, ***(13), (14), (15), (16),*** and***),also*** Several studies have indicated a link between the successful outcome of antiviral treatment and observed lipid metabolism parameters of the patient **(17).**

This study is a continuation of a previous work done by the same author on the evaluation of lipid profile in HCV cirrhotic and non cirrhotic patients **(18),** so this work is designed to study chronic hepatitis B and C VIRUSES

infections associated atherosclerosis and the pathogenic mechanisms operating in atherosclerotic cardiovascular and cerebrovascular diseases through measuring CIMT in attempets to develop a new strategy for early prediction, prevention and treatment of atherosclerotic complications in those patients. Most of the previous researches were a comparison studies between patients infected with HCV, HBV and healthy group with no regard to the presence or absence of cirrhosis in the infected group. The new point of view in this study is that it compare between infected non cirrhotics and infected cirrhotics .

About the demographic and laboratory data of the studied groups we found a statistically high significant difference as regard mean value ± SD of PLT, AST,ALT,GGT, HDL ($P \leq 0.001$) among the different groups of the study .A significant difference was found as regard mean value ± SD of WBCs, HB,PT, INR, S.albumin , T.cholestrol and LDL. ($P \leq 0.05$) .while no significant difference was found as regard mean value± SD of age (years),sex, total bilirubin and TGs ($P \leq 0.05$) .Because th liver is the central organ of lipid homeostasis for the entire body through the production of lipoproteins,major injuries to the hepatocytes such as those caused by chronic viral hepatitis or cirrhosis might produce abnormal liver function and decrease in levels of total cholestrol,triglyceride,LDL,HDL,…… **(19)**

In addition, **Haji et al., (20)** found the donor hepatitis C virus seropositivity is an independent risk factor for increase mortality and for the development of accelerated allograft vasculopathy after cardiac transplantation

In the previous study showed that HCV infection is associated with low serum lipid levels and lipid profile monitoring may help in the prediction of hepatic affection severity and its progression to liver cirrhosis **(21).**

One of the weakness of the previous study was, we did not include control subjects for comparison and we compared our results with the standardized laboratory data.

Despite all the above facts our present study interstingly,reveals that the mean values ± SD of serum total cholestrol,triglyceride and LDL is high in HBV,HCV infected patients when compared with control subjects. While the mean value ± SD of HDL is low in HBV,HCV infected patients than controls.

However,TC,TG and LDL mean values± SD are more or less similar to those in our previous study and still lower than that documented in the standradized laboratory indices. Despite our finding of relatively higher serum lipid profile individual values compared to controls, yet these values were still within the normal range.Furthermore,we have to stress that our chronic viral hepatitis patients were either non cirrhotic or compensated cirrhotics. This fact if considered in the light of the explanation of reduced serum lipids in chronic liver diseases as a reflection of deranged hepatic synthetic function and this is in concordance with(**Ghadir MR et al**)(22),could offer apossible rationalization.

Fujino T., et al.,(21) Hypothesized that HCV infection may contibute to triglyceride accumulation in the liver through transcriptional activation of lipogenic genes favoring lipid synthesis in those patients and this over expression of lipogenic genes may explain our finding.

Carotid intimal thickness values vary according to age and atherosclerosis-related risk factors, ranging from 0.60-0.75 mm (30-49 years) to 0.79-0.86 mm (50-79 years), **(12).**

A carotid plaque was defined as a focal thickening of ≥ 1.3 mm at the level of common carotid artery **(10).**

Adinolfi L.E., et al.,(23) Hypothesized that,the decreased cholesterol and LDL levels associated with HCV does not appear to translate into a cardioprotective role.Our results reveal that astatistically high significant increase in the mean values ± SD of carotid intimal thickness in HCV,HBV infected patients when compared with control subjects.

Also,in general ,the mean values SD of carotid intimal media thickness are statistically increased in non cirrhotic chronic hepatitic patients (both HBV,HCV) than cirrhotics 35% of HCV infected patients and 20% of HBV infected patients have carotid intima media thickness≥1.3 mm.

High significant correlations are found between CIMT and total cholestrol,triglyceride and LDL in both HCV &HBV infected patients. While non significant correlationswere found as regard HDL.Also no significant correlations were found between CIMT and PCR in both HCV&HBV infected patients.

Several possible mechanisms may exist to explain the relationship between HBV infection and atherosclerosis. First, HBV may colonize in the vascular tissues, leading to vascular damage. Second, HBV infection occasionally is associated with vasculitis. Third, chronic HBV infection may be associated with increased levels of oxidative stress, which may accelerate atherogenesis. Finally, chronic HBV infection may stimulate inflammatory and immune-mediated responses, (5)

HCV enters target cells through the LDL receptors and/or the scavenger receptor B1 **(24).** Some HCV proteins can cause oxidative stress with increased local reactive oxygen species **(25).**Additional viral characteristics may be involved, including an increased concentration of soluble intercellular adhesion molecules **(26)**, the appearance of anti-endothelial antibodies and the close association with vasculitis **(27).**

Our results are similarly encountredin other studies including;

Ishizaka et al., (28) suggested that HBsag positivity may be arisk factor for carotid atherosclerosis, while hepatitis C virus core protein sensitivity is independent predictor of carotid plaque and associated with carotid plaque and increased CIMT **(29).**

There was an association between hepatitis C virus seropositivity and coronary artery disease **(30).**

Chronic HCV infection can reduce the effectiveness of lipid-lowering therapy for carotid atherosclerosis (31).

Boddi et al., (32) found that the prevalence of intima-media thickness (>1mm) in carotid arteries was significantly higher in 31% of non cirrhotic HCV–positive patients.

While **Boddi et al., (33)** demonstrated the presence of HCV genomic sequences and replicative intermediates in plaque tissues, strongly suggesting the possibility of an active infection of carotid plaque.

Targher et al., (34), revealed that HCV infection is associated with early signs of atherosclerosis.

Nobukazu et al, (35) reported that carotid plaque was positive in (43%) and (28%) in HBV patients and control subjects respectively while **Petta et al (10)** found 41.9% of HCV patients compared to 40 % of control group had CIMT ≥1.3 mm.

In contrary to our results **Henry et al (36)** and **Arcari et al (37)** who concluded that was no association between HCV infection and atherosclerosis.

Yang et al ., (38) and **Reza et al., (39)** failed to find an association between chronic HBV infection and coronary atherosclerosis.

this difference could be explained by the difference of viral genotype in our country and number of patients included in the study also more advanced techniques have been introduced in the diagnosis of vascular diseases and viral load.

In conclusion,CIMT is increased in non cirrhotic chronic HCV&HBV infected patients and this increase is correlated with serum lipid profile parameters.And we suggested monitoring of lipid profile and CIMT in these groups of patients for early detection of atherosclerosis and early intervention to eliminate this sequale.

Conclusion:

In conclusion, our findings high prevalence that patients with chronic HCV, chronic HBV (in patients without cirrhosis and with a well-preserved liver function) are associated with early signs of atherosclerosis, independent of classical risk factors.

REFERENCES

1. **El Zanaty F et al 2009,WAY A.** Egypt demographic and health survey2008,Egypt Ministry of Health.Egypt;Cairo1-ZANATY and associates,andMacro international.,2009
2. **Mohlman et al., 2015, Brent Kobra,Kirti Shetty ,** BMC PUBLIC HEALTH 2015 15;1030
3. **Sharma et al .,Steele RW.Hpatitis B.** Available online http:emedicine.medscape.com(accessed on july 16.20110)
4. **El Shabrawi et al .,Mohamed F,Mona S,published in international journal of Tropical Diseases** &Health 3(2):157-168,2013
5. **De Maria-N, Colantonl A, Fagiuoli S, et al.** Association between reactive oxygen species and disease activity in chronic hepatitis C 1996. free Radfc Blol Med 1996;21:291-=295
6. **Ross et al** Atherosclerosis-an inflammatory disease. N Engl J Med **1999**; 340:115-126.
7. **Futterman LG, Lemberg L.** Fifty percent of patients with coronary artery disease do not have any of the conventional risk factors. Am J Crit Care **1998**; 7:240-244
8. **Epstein SE, Zhou YF, Zhu J** Infection and atherosclerosis: emerging mechanistic paradigms. Circulation. **1999;** 100(4):e20-8
9. **Camm AJ, Fox KM.** Chlamydia pneumonia (and other infective agents) in atherosclerosis and acute coronary syndromes. How good is the evidence? Eur Heart J. **2000**; 21(13):1046-51.
10. **Petta S,Torres D,Fazio G, et al** Carotid atherosclerosis and chronic hepatitis C aprospective study of risk associations.Hepatology 55:1317-1323
11. ***Targher G, Bertolini L, Padovani R, Poli F, Scala L, Zenari L, et al., (2006):*** Nonalcoholic fatty liver disease is associated with carotid artery wall thickness in diet-controlled type 2 diabetic patients. J Endocrinol Invest; 29:55–60.

12. **Touboul M. G. Hennerici, S. Meairs et al.,** "Mannheim carotid intima-media thickness consensus (2004–2006): an update on behalf of the advisory board of the 3rd and 4th Watching the Risk Symposium 13th and 15th European Stroke Conferences, Mannheim, Germany, 2004, and Brussels, Belgium,2006," Cerebrovascular Diseases, vol. 23, no. 1, pp. 75–80,2007.

13. **Thomson R, Bonk S, Thiele A.et al., (1993):** Density heterogeneities of hepatitis C virus in human sera due to the binding of B-lipoproteins and immunoglobulins. Med Microbiol Immunol; 182:329-334.

14. **Maggi G, Bottelli R, Gola D, et al. (1996):** Serumcholesterol and chronic hepatitis C. Ital J Gastroenterol 1996;28:436-440.

15. **Cicognani C, Malavolti M, Morselli-Labate AM, et al. (1997):** Serum lipid and lipoprotein patterns in patients with liver cirrhosis and chronic active hepatitis. *ArchIntern Med;157:792-796.*

16. **Fabris C, Federico E, Soardo G. et al., (1997):** Blood lipids of patients with chronic hepatitis differences related to viral etiology .Clin Chem Acta;261 :159-161.

17. **Serfaty L, Andreani T, Giral P.et al., (2001).** Hepatitis C virus induced hypobetalipoproteinemia: A possible mechanism for steatosis in chronic hepatitis C. J. Hepatol., 34,428-434

18. **Amal.Dewewdar , Usama M. Basha**,**Ahmed.Hussein**. B Evaluation of serum lipids profile in patients with chronic viral C hepatitis cirrhotic &non cirrhotic patients 2014

19. **Felmlee D.J, Sheridan D.A, Bridge S.H. et al. (2010).** Intravascular transfer contributes to postprandial increase in numbers of very-low-density hepatitis C virus particles. *Gastroenterology, 139, 1774-1783*

20. ***Haji SA, Starling RC, Avery RK, et al., (2004):*** donor hepatitis C- seropositivity is an independent risk factor for development accelerated coronary vasculopathy. J Heart Lung Transplant 23:277-283.

21. **Fujino T, Nakamuta M, Yada R. et al. (2010).** Expression profile of lipid metabolism-associated genes in hepatitis C virus-infected human *liver. Hepatol. Res. 40, 923-929.*

22. **Ghadir MR, Riahin AA, Havaspour A, et al., (2010):** The Relationship

between Lipid Profile and Severity of Liver Damage in Cirrhotic Patients . Hepat

Mon. Fall; 10(4):285-8.

23. **Adinolfi L.E., Restivo L, and Zampino R (2012):** Chronic HCV infection is a risk of atherosclerosis. Role of HCV and HCV-related steatosis. Atherosclerosis *221, 496-502.*

24. **Voisset C, Lavie M, Helle F. et al. (2005).** Ceramide enrichment of the plasma membrane induces CD81 internalization and inhibits hepatitis C virus entry. Cell Microbiol. 2008, 10, 606-617.

25. ***Tardif, K.D. Waris G.and Siddiqui, A. (2005):*** Hepatitis C virus, ER stress, and oxidative stress, Trends Microbiol 13 pp. 159–163

26. **Peng Ys,Chiang Ck,Hsu Sp et al .Influence of hepatitis C virus infection on soluble cellular adhesion molecules in hemodialysis patient.Blood purify 2005.,23:106-112[PMID:15640602 DOI:10.1159/000083204]**

27. **Zignego AL, Craxi A.et al.,** (**2008):** Extrahepatic manifestations of hepatitis C virus infection. Clin Liver Dis.; 12:611-36.

28. ***Ishizaka N., Ishizaka Y., Takahashi E., Tooda E., Hashimoto H.and Nagai et al., R. (2002):*** Association between hepatitis C virus seropositivity, carotid-artery plaque, and intima–media thickening, Lancet 359 pp. 133–135
29. ***Ishizaka Y, Ishizaka N, Takahashi E, Unuma T, Toonda E, Hashimoto H, et al., (2003):*** Association between hepatitis C virus core protein and carotid atherosclerosis. Circ J;67:26–30.
30. **Vassalle N**, Marković L. [Gene similarity between hepatitis C virus and human proteins-a blood transfusion problem]. *Med Pregl* 2005; **58**: 582-586 [PMID: 16673863 DOI: 10.2298/ MPNS0512582V]
31. ***Sawayama Y, Okada K, Maeda S et al., (2006):*** both Hepatitis C virus infection and chlamydia pneumonia are related to progression of carotid atherosclerosis . Fukuoka Igaku Zasshi 97:245-255.
32. **Boddi M,Abbate R,Chellini B.** HCV infection facilitates asymptomatic carotid atherosclerosis:preliminary report of HCV RNA localization in human carotid plaques.Dig liver Dis 2007;39 supp 1 :555-560
33. ***Boddi M, Abbate R et al., (2010):*** Hepatitis C virus RNA localization in human carotid plaques. Journal of clinical virology 47 72 – 75

34. ***Targher G 2007:*** Non-alcoholic fatty liver disease, the metabolic syndrome and the risk of cardiovascular disease: the plot thickens. Diabet Med 24: 1-6

35. **Nobukazu N,Takahashi E,et al .Association between hepatitis C virus seropositivity,Carotid plaque,and intima media thicknening.2002.,359:133-5**

36. **Henry P,Touboul M, Meairs et al.,** "carotid intima-media thickness consensus update on behalf of the advisory board of the 3rd and 4thWatching the Risk Symposium 13thand 15th European StrokeConferences, Mannheim, Germany,2004, Cerebrovascular Diseases, vol. 23, no. 1, pp. 75–80,2007.
37. ***Arcari CM, Nelson KE, Netski DM, Nieto FJ, Gaydos CA. (2006):*** No association between hepatitis C virus seropositivity and acute myocardial infarction. Clin Infect Dis;43:e53–e56
38. **Yang Kc,Chen MF,Su Tc etal,Hepatitis B virus seropositivity is not associated with increased risk of carotid atherosclerosis in Taiwanese.Atherosclerosis 2007.,195:392-397**
39. ***Reza G, Nasser A, Morteza G.*** Hepatitis B virus infection and the risk of coronary atherosclerosis. Ann Acad Med Singapore 37;913-5.