Relation of Hepatitis C and its Severity Assessed by PCR to the Presence and Severity of Coronary Artery Disease Assessed by Syntax Score

Thesis

Submitted for Partial Fulfillment of Master Degree in Cardiovascular Diseases

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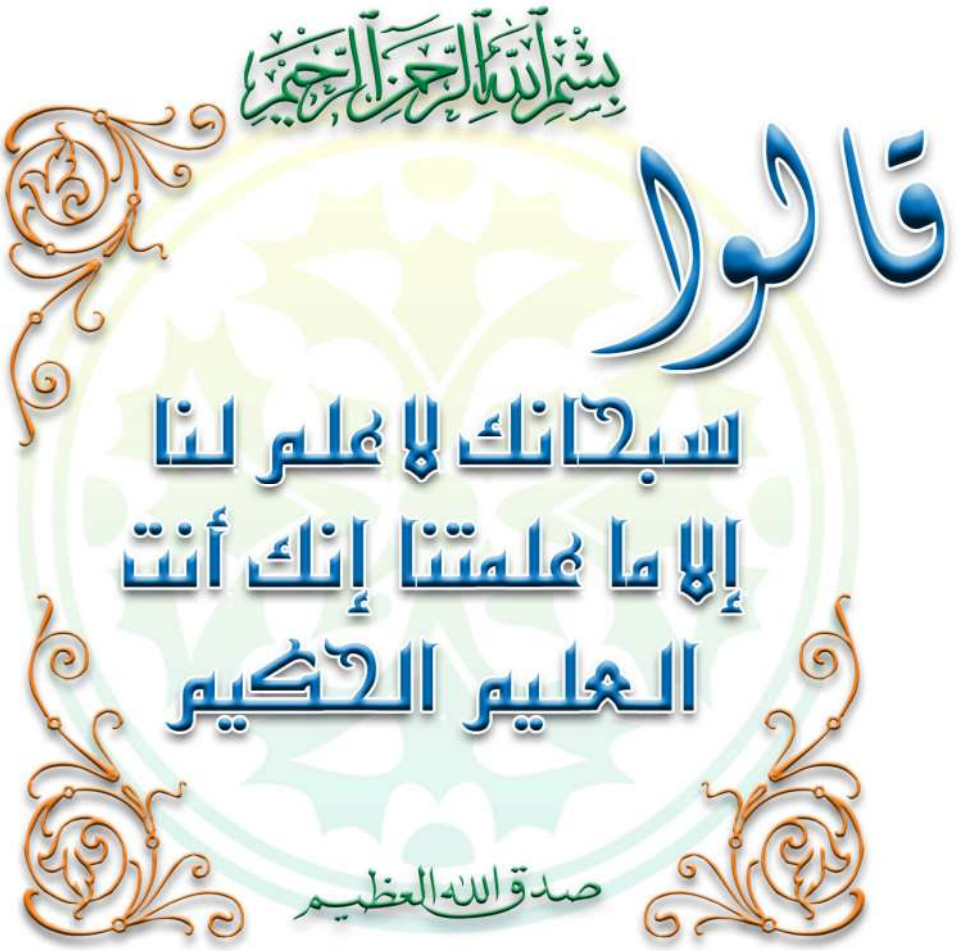
2018



سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to **ALLAH**,
the Most Kind and Most Merciful.

I'd like to express my respectful thanks and profound gratitude to **Dr./ Ahmed Mohamed Onsy,** *Assistant Professor of Cardiovascular Diseases Faculty of Medicine - Ain Shams University for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

I am also delighted to express my deepest gratitude and thanks to **Dr. / Adham Ahmed Abd Eltawab,** *Lecturer of Cardiovascular Diseases Faculty of Medicine - Ain Shams University, for his kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

Abd El-Salam Gebril Senussi

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List of Abbreviations

Abb.	Full term
ACS	*Acute coronary syndrome*
AHA	*Autoimmune hemolytic anemia*
ALT	*Alanine aminotransferase.*
AMI	*Acute myocardial infarction*
APO A	*Apoprotein A*
BMI	*Body mass index*
CAD	*Coronary artery disease*
CE	*Conformité Européennel European Conformity*
CGs	*Cryoglobulines*
CHD	*Coronary heart disease*
CRP	*C-reactive protein*
DM	*Diabetes Mellitus*
DNA	*Deoxyribonucleic acid*
EBCT	*Electron beam computed tomography*
EHM	*Extrahepatic manifestation*
ELISA	*Enzyme linked immune sorbent assay*
FDA	*Food and Drug Adminstration*
FR	*Free radical*
GGT	*Gamma glutamyltransferase*
HAV	*Hrpatitis A virus*
HBV	*Hepatitis B virus*
HCC	*Hepatocellular carcinoma*
HCV RNA	*Hrpatitis C virus ribonucleic acid*
HCV	*Hrpatitis C virus*
HIV	*Human immune deficiency virus*
HR	*Hazard Ratio*
hsCRP	*High sensitivity c-reactive protein*
IGg	*Immunoglobuline g*

List of Abbreviations Cont...

Abb.	Full term
IGm	*Immunoglobuline m*
IL	*Interleukin*
IMT	*Intima-Media thickness*
INF	*Interferon*
IR	*Insulin resistance*
kb	*Kilobase of nucleic acid*
LDL-C	*Low density lipoprptein cholesterol*
LP(a)	*Lipoprotein a*
LVEF	*Left ventricular ejection fraction*
MC	*Mixed cryoglobulinemia*
MI	*Myocardial infarction*
MTHFR	*Methylenetetrahydrofolate*
NHL	*Non Hodgkin lymphoma*
NO	*Nitric oxide*
OLT	*Orthotopic liver transplant*
OX LDL	*Oxidized LDL*
PCI	*Percutaneous coronary intervention*
PCR	*Polymerase Chain Reaction*
PCT	*Porphyria cutania tarda*
RNA	*Ribonucleic acid.*
RT-PCR	*Reverse transcriptase PCR*
SS	*SYNTAX SCORE*
SVR	*Sustained virologic response*
TMA	*Transcription mediated amplification*
TNF-a	*Tumor necrosis factor-a.*
UTR/NTR	*Un/non translated region*
WHO	*World Health Organization.*

INTRODUCTION

Hepatitis C has been declared as a global health problem by the World Health Organization, with about 3% of the world's population (roughly 170-200 million people) infected with HCV***(Lauer and Walker, 2001).***

Approximately 150 million people worldwide have chronic hepatitis C infection, roughly 1 person in 50 is infected with the hepatitis C virus ***(World Health Organization, 2015).***

Egypt has the highest prevalence rate of hepatitis C virus in the world, making it the most challenging public health problem facing the country ***(ESMAT et al., 2013).***

Studies show that 14.7% of the Egyptian population carry HCV antibodies and 9.8% have an active infection ***(El.Zanaty et al., 2009).***

The association between hepatitis C virus (HCV) infection and coronary artery disease (CAD) is controversial. Some studies have reported no association between HCV infection and CAD, whereas others have reported an increased risk. Very recent data have indicated that HCV infection was associated with a higher risk of CHD, after the adjustment of traditional risk factors, and seropositivity for HCV may have a role in the pathogenesis of carotid atherosclerosis, furthermore; HCV infection may independently predict an increased severity of CHD ***(Butt et al., 2009).***

There is some evidence for variation in the course of infection assosciated with different HCV variants (genotypes) and in response to treatment with interferon ***(Kanai et al., 1991).***

In the Middle East almost all anti-HCV positive individuals are infected with type 4 ***(Simmond et al., 1993).***

As individuals with HCV begin to age, they will inevitably face common comorbidities such as cardiovascular diseases. It is unknown how infection with HCV affects coronary heart disease (CHD) progression and outcomes ***(Armstrong et al., 2006)***.

Infectious etiologies have been hypothesized to contribute to the inflammatory cascade leading to atherosclerosis ***(Danesh et al., 1997).***

Aim of the Work

The aim of this study is to assess the correlation between hepatitis C virus infection severity and extent of coronary artery disease among patients presenting to Ain Shams University cath lab for coronary angiography or PCI.

Chapter 1

HEPATITIS C

Epidemiology

Hepatitis C is a disease of great global impact. According the **World Health Organization** there are more than 100 million people chronically infected with the hepatitis C virus(HCV),corresponding to 2-2.5% of the world total population. There are great regional differences. In some countries e.g., Egypt, the prevalence is more than 10% ***(WHO 2014).***

The incidence of HCV infections is difficult to be determined, because most acute cases are not observed clinically. Less than 25% of acute cases of hepatitis C are clinically apparent ***(Vogel et al., 2009).***

A recent study In Egypt showed that about one person in seven of Egypt's 83 million populations tested positive for HCV antibodies, indicating that these individuals have been infected with the virus at some point. However, approximately one person in ten carries HCV RNA and is therefore chronically infected ***(El-Zanaty et al., 2009).***

This means a very large viral reservoir is fuelling the spread of the disease among Egyptians, mainly through hospitals and clinics (hospitals and dental, private clinics).

Fixed data for the infection rate are hard to come by. A study in 2010 estimated that the number of new cases is more than half a million peoples each year. However, the Egyptian Ministry of Health and Population (MOHP) puts the number at 100,000 per year. Both numbers should be much lower ***(Miller et al., 2010).***

HCV problem in EGYPT is not only about size, but also the genotype of the virus in circulation is one that is not commonly found in the rest of the world ***(Miller et al., 2010).***

An epidemic spread of HCV has been suggested because of the very noticable homogeneity of HCV subtypes found in Egypt (mostly 4a). Since a history of injection treatment has been suggested as a risk factor for HCV, a prime candidate to explain the high prevalence of HCV in Egypt is the past practice of parenteral therapy for bilharziasis. The large reservoir of chronic HCV infection settled in the course of these campaigns remains likely to be responsible for the high prevalence of HCV morbidity and may be largely responsible for the continued endemic transmission of HCV in Egypt today ***(Lavanchy et al., 2000).***

HCV Infection occurs throughout the world, and up until the introduction of anti-HCV screening tests for blood donors, introduced in 1990/1991 in Europe and the United States, it has represented the major cause of transfusion-relateds hepatitis ***(Van der Poel, 1999).***

Injecting drug users have very high rates of HCV antibody reactivity (>70%). on the other hand Intermediate prevalence of about 20 to 30% have been found in patients receiving hemodialysis. The incidence is declining since transmission by blood products has been reduced to almost zero and universal precautions in medical settings are followed ***(EASL International Consensus Conference on Hepatitis C 1999).***

Transmission

The most important way of transmission of HCV infection is parenteral exposure to the virus.The majority of infection with HCV in Europe and the US occurred through intravenous drug use or blood transfusion. The latter has become rare since routine testing of the blood supply for HCV began in the early 1990s. Other types of parenteral exposure are important in specific regions in the world. The following possible routes of infection have been identified in anti-HCV positive blood donors (in descending order of transmission risk): − Injection drug use − Blood transfusion − Sex with an intravenous drug user − Having been in jail more than three days − Religious scarification − Having been struck or cut with a bloody object − Pierced ears or body parts − Immunoglobulin injection. Very often in patients with newly diagnosed HCV infection no clear risk factor can be identified.

Injection drug use

The commonest source of acute HCV infection is injection drug use. It is estimated that most newly acquired infections occur in individuals who have injected illicit drugs. The prevalence of anti-HCV antibodies among groups of intravenous drug users may be up to 70% with significant variation based on factors such as region, risk behaviour, socioeconomic status, etc, underscoring the efficiency of transmission via direct blood contact ***(Sutton, 2008).*** HCV infection also has been associated with a history of intranasal cocaine use, presumably due to blood on shared straws or other sniffing paraphernalia. This may explain partly the recent increase in cases of acute HCV infections in HIV+ MSM ***(Schmidt, 2011; Rockstroh, 2012)***, although both WHO and CDC now recognise sex as a transmission route.

Blood transfusion

In some historic cohorts 10% or more of patients who received blood transfusions were infected with hepatitis C ***(Alter, 1989).***

Although, blood transfusion or use of other blood products was a major risk factor for transmission of HCV in the past, screening of blood donor for HCV since the early 1990s has nearly eliminated this route of transmission. Blood donors are screened for anti-HCV antibodies and HCV RNA at least in