

***Prevalence of Hepatitis C Virus among Egyptian
Patients admitted to the Rheumatology
Department in el Kasr el Aini Hospital***

*Thesis submitted for fulfillment of the M.Sc. degree in Rheumatology and
Rehabilitation*

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Dedication

To my family, who supported me throughout my life, I dedicate this work to you all, thanks a lot. Special thanks to my dad and my professor whose endless love and guidance made this work possible.

Abstract

Aim of the work:

The aim of this work is to study the prevalence of HCV among patients admitted to the rheumatology ward, Rheumatology and Rehabilitation Department, Cairo University hospitals.

Patients and Methods:

157 patients admitted to the rheumatology Department, Cairo University between January 1st and June 30th, 2009 were included in this study. All of them were subjected to the following:

- Detailed History taking and thorough clinical examination, routine laboratory data including ESR, CBC, liver function tests, kidney function tests and auto-antibodies.*
- All patients were screened for HCV antibodies (Anti-HCV) using ELISA technique, when needed, other laboratory tests such as HCV-RNA, cryoglobulins etc, were done.*

Results:

29 out of 157 patients (18.5%) were positive for HCV antibody. 18 patients of them (62%) were admitted primary due to rheumatic disease and concomitantly associated with HCV antibodies. On the other hand, 11 patients (38%) were admitted mainly due to rheumatic extra-hepatic manifestations, which represent 7% of all patients admitted to the Rheumatology ward during the time period of the study. Arthritis, palpable Purpura, digital gangrene, mononeuritis multiplex were the most common causes of admission related to chronic HCV infection. 71.4% of patients with positive HCV antibody had active viremia (positive PCR-RNA).

Conclusion:

Chronic HCV infection represents a leading cause of admission to the rheumatology ward, Cairo University Hospitals. Increased awareness with the problem of HCV is needed among rheumatologists dealing with Egyptian patients.

Keywords

HCV

prevalence

Rheumatology ward

Egypt

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List of Abbreviations

<i>AASLD</i>	American Association for the Study of Liver Diseases
<i>ACPA</i>	Anti citrulline peptide antibody
<i>ACR</i>	American College of Rheumatology
<i>AFP</i>	Serum alpha fetoprotein
<i>ALP</i>	Serum alkaline phosphatase
<i>ALT</i>	Serum alanine transaminase
<i>AMA</i>	Antimitochondrial antibodies
<i>ANA</i>	Anti-nuclear antibody
<i>ANCA</i>	Anti-neutrophil cytoplasmic antibody
<i>Anti- RNP</i>	Ribonucleoprotein complex
<i>Anti-HBc</i>	Anti-hepatitis B core antibodies
<i>Anti-LKM-1</i>	Anti-liver-kidney microsome antibodies
<i>AOSD</i>	Adult onset Still's disease
<i>APS</i>	Antiphospholipid syndrome
<i>AST</i>	Serum aspartate transaminase
<i>bDNA</i>	Branched-chain DNA assays
<i>C3</i>	Complement 3
<i>CCP</i>	Cyclic citrullinated peptide
<i>CT</i>	Computed tomography
<i>ECG</i>	Electrocardiogram
<i>EIA</i>	Enzyme immunoassay
<i>ELISA</i>	Enzyme-linked immunosorbent assay
<i>ENA</i>	Extractable nuclear antigen
<i>ESR</i>	Erythrocyte sedimentation rate
<i>EVR</i>	Early virologic response
<i>FDA</i>	Food and drug administration.
<i>FM</i>	Fibromyalgia
<i>GGT</i>	Gamma glutamyl transferase
<i>HBsAg</i>	Hepatitis B surface antigen

<i>HBV</i>	Hepatitis B virus
<i>HCC</i>	Hepatocellular carcinoma
<i>HCV</i>	Hepatitis C virus
<i>HIV</i>	Human immunodeficiency virus
<i>HRCT</i>	High resolution Computed Tomography
<i>HTLV</i>	Human T lymphotropic virus
<i>IFN</i>	Interferon
<i>IGF</i>	Insulin-like growth factor
<i>IgG, IgM, IgA</i>	Immunoglobulin G, M, A
<i>IPF</i>	Interstitial pulmonary fibrosis
<i>ITP</i>	Immune thrombocytopenic Purpura
<i>IVDU</i>	Intravenous drug users
<i>JIA</i>	Juvenile idiopathic arthritis
<i>LP</i>	Lichen planus
<i>MC</i>	Mixed cryoglobulinemia
<i>MCTD</i>	Mixed connective tissue disease
<i>MG</i>	Myasthenia gravis
<i>MPGN</i>	Membranous proliferative glomerulonephritis
<i>MRI</i>	Magnetic resonance imaging
<i>NAT</i>	Nucleic acid testing
<i>NHANES</i>	National Health and Nutrition Examination Survey
<i>NHL</i>	Non-Hodgkin lymphoma
<i>PAN</i>	Polyarteritis nodosa
<i>PAT</i>	Parenteral anti-schistosomal therapy
<i>PCR</i>	Polymerase chain reaction
<i>PCT</i>	Porphyria cutanea tarda
<i>PM/DM</i>	Polymyositis/dermatomyositis
<i>PSS</i>	Progressive systemic sclerosis
<i>PTH</i>	Parathormone
<i>RA</i>	Rheumatoid arthritis
<i>RF</i>	Rheumatoid factor

<i>RIBA</i>	Recombinant immunoblot assay
<i>RT-PCR</i>	Reverse transcriptase polymerase chain reaction
<i>RVR</i>	Rapid virologic response
<i>SLE</i>	Systemic lupus erythematosus
<i>SS</i>	Sjogren's syndrome
<i>TMA</i>	Transcription-mediated amplification
<i>TMB</i>	Chromogen tetramethylbenzidine
<i>UROD</i>	Enzyme uroporphyrinogen decarboxylase
<i>WHO</i>	World Health Organization

Introduction and aim of the work

Hepatitis C virus (HCV) is a global pathogen, infecting an estimated 170 million people worldwide, and is the most common blood-borne viral infection in the United States. It has been estimated that 3.9 million Americans have been exposed to the virus, with 2.9 million believed to be chronically infected [Rustgi, 2007].

In Egypt the situation is quite worse. Egypt has the highest prevalence of hepatitis C in the world. The national prevalence rate of HCV antibody positivity has been estimated to be between 10-13% [Mohamed, 2004]. In one study, sera were obtained from 3608 blood donors at 13 governorates in or surrounding the Nile valley during 1999. Antibody to HCV (anti-HCV) was found in 317 (8.8%) of them [Tanaka et al., 2004], compared to the prevalence of antibodies to HCV (anti-HCV) in the United States which is approximately 1.6 percent according to the most recent National Health and Nutrition Examination Survey [Armstrong et al., 2006].

The hepatitis C virus (HCV) is a cause of both acute and chronic hepatitis. In addition, several extra-hepatic diseases have been associated with chronic HCV infection, and in most cases appear to be directly related to the viral infection. These include: arthralgia, arthritis, myalgia, cryoglobulinemic vasculitis, secondary Sjogren's syndrome, thyroiditis, generation of autoantibodies, renal disease, dermatologic conditions such as lichen planus and porphyria cutanea tarda [Pawlotsky et al., 1994; Gumber and Chopra, 1995; Cacoub et al., 2000; El-Serag et al., 2002] . In one series of 321 patients, at least one extra-hepatic manifestation was observed in 38 percent [Cacoub et al., 2000].

Rationale and aim of the work:

Egypt has higher rates of HCV than neighboring countries as well as other countries in the world with comparable socioeconomic conditions and hygienic standards for invasive medical, dental, or paramedical procedures. Chronic HCV infection is commonly associated with extra-hepatic manifestations; many of them are related to rheumatology practice.

Accordingly, the aim of this work is to study the prevalence of HCV among patients admitted to the rheumatology ward, Cairo University Hospitals.

Review of Literature

CHAPTER I

Hepatitis C Virus Infection

CHARACTERISTICS OF HCV

It became apparent after the discovery of the hepatitis A and B viruses in the late 1960s and early 1970s that a large proportion of cases of acute and chronic hepatitis could not be explained by either of these agents. Another viral agent was suspected, and patients infected with this suspected agent were said to have non-A, non-B hepatitis. The agent was finally identified in 1989 when the genome of the virus was cloned and the agent was designated the hepatitis C virus (HCV) [Choo et al., 1989].

The hepatitis C virus particle consists of a core of genetic material (RNA), surrounded by an icosahedral protective shell of protein, and further encased in a lipid (fatty) envelope of cellular origin. Two viral envelope glycoproteins, E1 and E2, are embedded in the lipid envelope [Op De Beeck and Dubuisson, 2003].

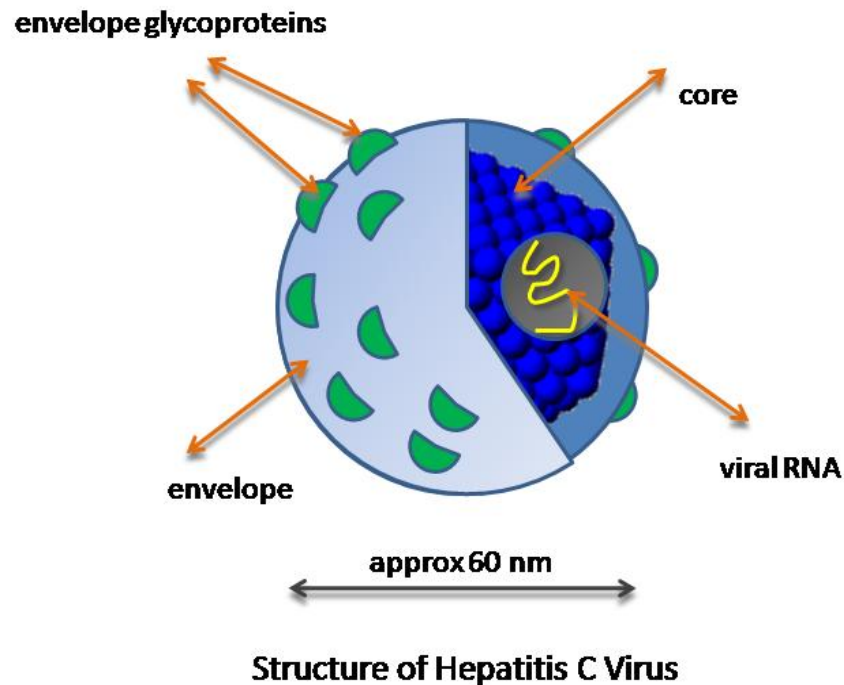


Figure 1: Structure of HCV

The hepatitis C virus is a small 40 to 60 nm virus with a lipid envelope and a single-stranded RNA viral genome comprising approximately 9500 nucleotides [Houghton et al., 1991]. It belongs to the Flaviviridae family. It has extensive genomic variability resulting in six major genotypes [Simmonds et al., 1994, Major and Feinstone, 1997, and Bartenschlager and Lohmann, 2000]. More than 50 subtypes have also been described; the most common subtypes are 1a, 1b, 2a, and 2b [Simmonds et al., 2005]. Replication of HCV is "error-prone". In addition, the evolution of genotypes has probably been influenced by several factors, including immune selection, infection patterns, replication efficiency, and population migration. Thus, there is a distinct geographic distribution of HCV genotypes [Dusheiko et al., 1994 and Lau et al., 1996]. Genotype 1 is most common (60 to 70% of isolates) in the United States and Europe [Dusheiko et al., 1994 and Lau et al., 1996]; genotypes 2 and 3 are less common in these areas,

while genotypes 4, 5, and 6 are rare: Genotype 3 is most common in India, the Far East, and Australia. Genotype 4 is most common in Africa and the Middle East and appears to be emerging more frequently in Europe among intravenous drug users and homosexuals. Possibly related to immigration to Europe from North Africa, Genotype 5 is most common in South Africa and Genotype 6 is most common in Hong Kong, Vietnam, and Australia. Although subtype 4a is the dominant Egyptian HCV strain, a survey by Ray et al., 2000, of HCV genetic diversity in the country revealed that other subtypes (provisionally named 4a, 4b, and 1g) are also present at lower prevalence.

The clinical significance of viral genotypes is not entirely clear, but they have a significant effect upon the response to interferon-based therapy. The sustained virologic response to pegylated interferon plus ribavirin ranges from about 40 to 50% with genotype 1 (including 1a and 1b) to as high as 70 to 80% with genotypes 2 and 3 [Martinot-Peignoux et al., 1995 and Davis and Lau, 1997].

EPIDEMIOLOGY

Hepatitis C virus infection occurs throughout the world and affects about 3% of the world's population [Cacoub et al.1999]. The Centers for Disease Control estimates that the number of new cases of acute hepatitis C virus (HCV) infection in the United States has fallen from approximately 230,000 per year in the 1980s to its current level of about 19,000 cases per year [Wasley et al., 2006]. The overall incidence in 2006 was estimated to be 0.3 to 100,000 [Wasley et al., 2006]. The decline relates primarily to reduction of infection in injection drug users, a probable consequence of changes in injection practices motivated by a concern for HIV risk. The number of cases of transfusion-associated acute hepatitis C decreased significantly after 1985 and has been reduced almost to zero [Alter, 1997]. Thus,