

**UI ;rRsk factors of hepatitis C among patients of  
Theodor Bilharz Research Institute**

**Thesis**

*Submitted for fulfillment of M.Sc Degree in Public Health*

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**2009**

## **,Acknowledgement**

*At the beginning thanks to Allah, most gracious and most merciful, without his great blessing I would have never accomplished this work.*

*I would like to express my deepest thanks to my supervisors. I wish to express my deepest thanks and gratitude to **Professor Naffousa Ali Affify**, Professor of Public Health Faculty of Medicine Cairo University.*

*Her expert guidance, invaluable criticism and constant encouragement have helped me in the progress of this work.*

*I am greatly indebted to **Dr.Shymaa Baher Ismail**, Lecturer of Public Health Faculty of Medicine Cairo University, for sparing so much of her valuable time, for her esteemed criticism and expert advice.*

*I would also like to thank **Dr.Howaida Hamed El Desouky**, Lecturer of Public Health Theodor Bilharz Research Institute for her invaluable and endless help and practical contribution to this study.*

*I wish to extend my thanks to the Blood Bank team, the Tropical team and to all those who assisted me to complete this work at Theodor Bilharz Research Institute. My deepest gratitude to my patients who participated and helped me to implement this study.*

*Finally, I express my thanks and gratitude to my family for their wonderful and endless support.*

## **Abstract**

HCV disease is a major health problem of Egypt with a prevalence of 10- 18%. A case control study was carried out among attendants of Theodor Bilharz Research Institute to clarify the role of risk factors (RF) in the spread of hepatitis C virus (HCV) infection. All subjects were contacted by interviewer, that completed a questionnaire. Their sera were collected and tested for HCV antibodies. (100) subjects, positive for anti-HCV (cases) were compared with (150) controls that tested negative for anti-HCV, Gender and age were matched. The risk factors were statistically compared by univariate and multivariate analysis. The study proved significant difference and risk of infection of the following variables: residence, education, occupation, socioeconomic score, contact with canal water, Bilharzial infection, tartar emetic injection, hospital admission, department of admission, blood and blood product transfusion and their places, veinsection and its place, dental management and its place, family hepatitis and the diseased member, sharing equipment and its place, circumcision and its place, sewage disposal and source of water.

## **Keywords**

**Hepatitis C, risk factors**

## /Contents

<b>I. INTRODUCTION</b>	1
<b>II. AIM OF WORK</b>	3
<b>III. GOAL</b>	3
MAIN OBJECTIVES	3
SUB OBJECTIVES	3
<b>IV. REVIEW OF LITERATURE</b>	4
<b>CAUSES OF VIRAL HEPATITIS</b>	4
<b>HEPATITIS C VIRUS</b>	5
<b>EPIDEMIOLOGY</b>	5
NATURAL HISTORY AND DISCOVERY OF HCV	5
VIROLOGY	6
TYPES OF HEPATITIS C VIRUS	8
GLOBAL DISTRIBUTION OF HCV	9
ORGANISM SENSITIVITY OUTSIDE THE BODY	10
<b>MODE OF TRANSMISSION (RISK FACTORS)</b>	10
<i>PARENTAL TRANSMISSION</i>	10
<i>NON-PARENTAL RISK FACTORS</i>	13
<i>NOSOCOMIAL INFECTION</i>	19
<b>PATHOGENESIS OF HCV LIVER DISEASE</b>	21
<b>PATHOGENESIS OF EXTRAHEPATIC MANIFESTATIONS</b>	24
<b>CLINICAL PICTURE:</b>	24
<i>INCUBATION PERIOD</i>	24
<i>ASYMPTOMATIC INFECTION</i>	24

<i>ACUTE HCV INFECTION</i>	24
<i>CHRONIC HCV INFECTION</i>	25
<i>EXTRA HEPATIC MANIFESTATIONS</i>	26
<i>COMPLICATIONS</i>	26
<b>DIAGNOSIS OF HCV</b>	28
<b>BURDEN OF THE DISEASE</b>	31
<b>PREVENTION AND CONTROL OF HCV INFECTION:</b>	32
<b>PRIMARY PREVENTION</b>	33
<b>SECONDARY PREVENTION</b>	50
<b>INTERNATIONAL EFFORTS FOR PREVENTION OF HEPATITIS C</b>	50
<b>TREATMENT OF HCV INFECTION</b>	54
<b>TREATMENT OF SPECIAL SITUATIONS</b>	56
<b>V.SUBJECTS AND METHODS</b>	58
<b>VI.RESULTS</b>	66
<b>VII.DISCUSSION</b>	106
<b>VIII.CONCLUSIONS &amp; RECOMMENDATIONS</b>	117
<b>IX.SUMMARY</b>	120
<b>X.REFERENCES</b>	123
<b>XI.ANNEX</b>	144
<b>XII.ARABIC SUMMARY</b>	146

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## List of tables

*Table(1):Distribution of cases and control according to age groups*

*Table (2):Distribution of cases and controls according to sex*

*Table(3): Distribution of cases and controls according to marital status*

*Table(4a): distribution of cases and controls according to residence*

*Table(4b): distribution of cases and controls according to residence*

*Table (5a):Distribution of cases and controls according to education*

*Table (5b):Distribution of cases and controls according to education*

*Table (6): distribution of case and control according to their occupation*

*Table (7): distribution of cases and control according to Socioeconomic score*

*Table (8): distribution of cases and control according to hazardous occupation*

*Table(9) : Distribution of cases and controls according to previous contact with Canal water*

*Table(10) :distribution of cases and controls according to previous bilharziasis infection*

*Table (11):Distribution of cases and controls according to history of tartar emetic Injection*

*Table (12): Distribution of cases and controls according to needle prick*

*Table (13): Distribution of cases and controls according to hospital admission*

*Table (14): Distribution of cases and controls according to the department of admission*

*Table(15):distribution of cases and controls according to history of blood transfusion*

*Table(16) : Distribution of cases and controls according to place of blood transfusion*

*Table(17) : History of blood product transfusion among sample type*

*Table (18):Distribution of cases and controls according to place of blood product transfusion*

*Table (19): Distribution of cases and controls according to history of vein section*

*Table (20): Distribution of cases and controls according to Place of vein section*

*Table (21): Distribution of cases and controls according to history of dental management*

*Table (22):Distribution of cases and controls according to place of dentist*

*Table (23):Distribution of cases and control according to Family history of hepatitis*

*Table (24): Member of the family diseased with hepatitis according to type*

*Table(25) :distribution of cases and controls according to Partner with hepatitis*

*Table (26): Distribution of cases and controls according to History of sharing equipment*

*Table (27): Distribution of cases and controls according to site of sharing equipments*

*Table(28) : Distribution of cases and controls according to illegal sex*

*Table (29a) : distribution of cases and controls according to place of circumcision*

*Table (29b) :distribution of cases and controls according to place of circumcision*

*Table (30): Distribution of cases and control according to history of tattooing*

*Table (31): Distribution of cases and controls according to rate of solid waste disposal*

*Table (32): Distribution of cases and controls according to type of Sewage disposal*

*Table (33): Distribution of cases and controls according to source of Water*

*Table(34):logistic regression analysis*

## List of figures

*Fig.(1)HCV by electron microscopy*

*Fig.(2) Hepatitis c transmission*

*Fig.(3)Decontamination Steps*

*Fig.(4)Relation between type of item & its decontamination*

*Fig.(5)Steps of Medical- Waste Management*

*Fig.(6)Burial pit*

*Fig.(7)Incinerator*

*Fig.(8) Showing relation between cases and controls according to age groups*

*Fig.(9) Showing relation between cases and controls as regards occupation:*

*Fig.(10) Showing relation between cases and controls as regards blood transfusion*

*Fig.(11) Showing relation between cases and control as regards history of sharing equipments*

*Fig.(12) Showing relation between cases and controls as regards place of sharing equipments*

*Fig.(13) distribution of cases and control according to type of sewage disposal*

*Fig.(14)percent of cases and control according to water source*

## Abbreviations

• HCV	Hepatitis C virus
• HCC	Hepatocellular carcinoma
• TTV	Transfusion transmitted virus
• HGV	Hepatitis G virus
• SARS	Severe acute respiratory syndrome
• NANBH	Non-A non-B hepatitis
• RNA	Ribonucleic acid
• Nm	Nanometer
• 5'UTR	5' Untranslated region
• Nt	nucleotides
• IRES	Internal ribosomal entry site
• PCR	Polymerase chain reaction
• 5'NCR	nucleotides coding region 5'
• ELISA	Enzyme Linked Immunosorbant Essay
• AHC	Acute hepatitis C
• IDUs	Injection drug users.
• PAT	Parenteral antischistosomal therapy
• HBV	Hepatitis B virus
• RT-PCR	Transcriptase–polymerase chain reaction
• HVL	High virus load
• HIV-1	Human immunodeficiency virus type 1
• CRF	Chronic renal failure
• ESRD	End-stage renal disease
• NK	Natural killer
• CD8+	Cytotoxic Tcells
• IFN	Interferon
• ALT	Alanine transferase
• <i>PCT</i>	porphyria cutanea tarda
• TMA	Transcription mediated amplification

<ul style="list-style-type: none"> <li>• EIA</li> <li>• FT-AT</li> <li>• CLD</li> <li>• SP</li> <li>• IC</li> <li>• PPE</li> <li>• HLD</li> <li>• STRIVE</li> <li>• CDC</li> <li>• STD</li> <li>• TB</li> <li>• NCHHSTP</li> <li>• PEG</li> <li>• SVR</li> </ul>	<p>Electroimmunosorbantantibodies</p> <p>FibroTest ActiTest</p> <p>Chronic liver disease</p> <p>Standard precautions</p> <p>infection control</p> <p>Personal protective equipment</p> <p>High level disinfection</p> <p>Study to Reduce Intra-Venous Exposures</p> <p>Centers for Disease Control and Prevention</p> <p>Sexually transmitted disease</p> <p>Tuberculosis</p> <p>National Center for HIV, Viral Hepatitis, STD, and TB Prevention</p> <p>polyethylene glucol</p> <p>Sustained virological response</p>
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## Review of literature

### Causes of Viral hepatitis:

Some hepatic viruses such as hepatitis A, B, C, D and E are well clearly identified and molecularly defined as hepatotropic agents which have no major pathologic involvement of other organs ( *Thomas et al., 1997*). However, despite the identification of these viruses, the etiology of 5 – 20 % of acute post-transfusion and community acquired hepatitis, and more than 40% of fulminate hepatitis cases are of unknown etiology (*Cheung and keeffe 1997*). The hepatitis G virus belongs to Flaviviridae family but it is clearly distinct from hepatitis C virus (*Muerhoff et al. 1995*). It was detected in 48% of acute hepatitis C infection (*Romano et al. 2000*) Transfusion transmitted virus (TTV) also implicated in transfusion associated hepatitis (*Naoumov et al. 1998*), causal association of HGV or TTV with hepatitis has not been confirmed in serum studies ( *Naoumov et al. 1998*). hepatic injury caused by corona virus was described recently as a cause of severe acute respiratory syndrome (SARS) –associated viral hepatitis (*Chau et al. 2004*).

## **Hepatitis c virus**

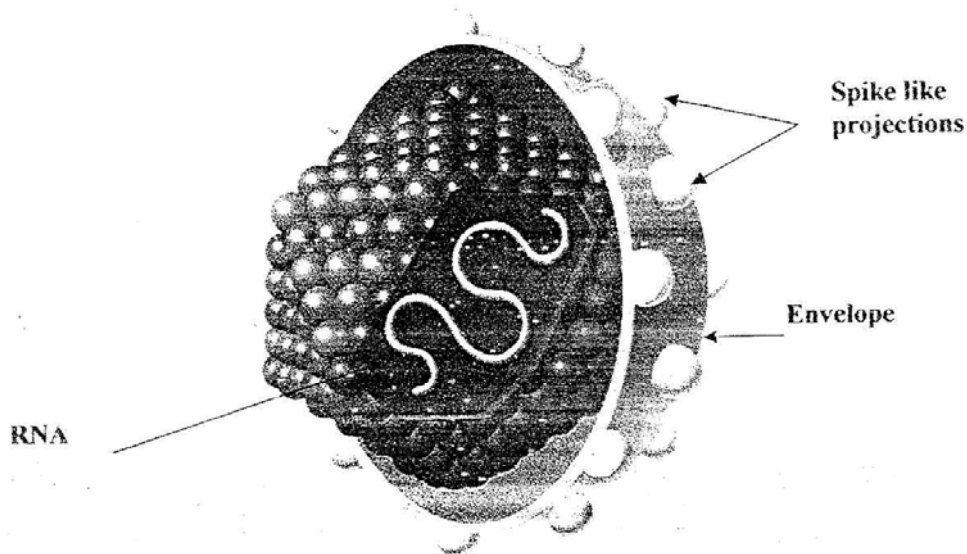
### **Epidemiology:**

#### **Natural history and discovery of HCV:**

The recognition of the specific viral agents responsible for hepatitis B and A was made in 1970, although most cases of post transfusion hepatitis could not be explained by either the hepatitis A or hepatitis B virus and it was initially called non-A non-B hepatitis (NANBH) (*Dane et al., 1970*). Several studies succeeded in transmission of NANB hepatitis through blood from transfusion associated hepatitis patients to chimpanzees and therefore clearly demonstrated that the disease was the result of a transmissible agent ( *Bradley et al., 1979*). HCV was detected and isolated as a single stranded RNA virus in 1989 and was responsible for most transfusion-associated non-A non-B hepatitis and have been named hepatitis C virus (*Choo and Kuo et al., 1989*). Identification of the non A non B hepatitis virus was finally accomplished in 1988 by *Houghton et al.*, from Chiron corporation (Emery Ville, California) and by Bradley at CDC who first characterized and cloned the agent by molecular biologic assays before it was ever visualized or isolated in cell culture and named it HCV (*Choo et al., 1989*).

## **Virology:**

Different attempts to visualize the infectious HCV particle have been largely unsuccessful (*Thomson and Liang ,2000*), this can be attributed to the low level of the virus in plasma samples and problems of in vitro cultivation (*Shimizu et al .,1996*).Hepatitis c virus is an enveloped virus, approximately 50 nm in size consists of appositve sense ,single stranded RNA genome within a nucleocapsid (fig.1),which is encased in an envelope derived from host membranes into which viral encoded glycoproteins are inserted(*Choo et al., 1991*).



**Fig. I**  
**HCV by electron microscopy**

Studies on HCV- positive sera and plasma have isolated both low- and high – density fractions containing HCV RNA .The association with low density lipoproteins

may be responsible for the low- density fraction while the higher- density fraction possibly represents free virus or particles complexed with immunoglobulin (*Choo et al., 1995*). Association with low-density lipoproteins can potentially confer two advantages to the virus:

1-It may protect particles from antibody-mediated neutralization .

2-Virions may gain entry into cells via cellular low- density lipoprotein receptor.

The higher –density fraction exhibited low infectivity compared with the low – density one which is highly infectious (*Hijikata et al.,1993*).

By constant mutation, HCV may be able to escape host immunologic detection. As a consequence , most HCV-patients develop chronic infection (*Lemon et al.,1995*).HCV also knocks out the host's innate immunity(*Foy,2003*).

HCV genome is classified with in a separate novel genus hepacivirus in the family Flaviviridae ( *Robertson et al.,1998*). *Kaito et al.,1994*; By immune electron microscopy showed that HCV particles are 55 to 65 nm diameter spherical particles with fine surface spike-like.

The 5 Untranslated region (5UTR) is a 341 nucleotides (nt) sequence and contains sequence elements necessary for replication and for directing viral protein synthesis(*Bukh 2000*).there is a segment acting as an internal ribosomal entry site (IRES) binding to the ribosomes of the infected cell and allowing translation of viral protein( *Honda et al.1996*).Genotype specific variations in the 5 UTR has facilitated the development of PCR and based genotyping methods(*Thomson and Liang 2000*). The 3 UTR consists of a relatively variable 30 nt segment at the 3 terminus of the polyprotein- coding region. In the extreme 3 terminus there is the most conserved segment of HCV genome which is known as x region( *Di Bisceglie 1999*). The heterogeneity hinders the development of vaccines ( *Houghton et al., 1996*).

### **Types of hepatitis c virus**

HCV displays significant genetic heterogeneity as a result of accumulation of mutations during replication. The genetic heterogeneity is not uniform across the genome, the most highly conserved regions of the genome are parts of the nucleotides coding region 5'(5'NCR) and the terminal 3'NCR followed by the core region. In contrast, the most heterogeneous portions of the genome are the genes encoding the envelope proteins (E1 and E2). (*Kato, N., 2001*) Accumulation of nucleotide substitution in the HCV genome results in diversification and evolution into different genotypes, subtypes and quasispecies. No fewer than 6 genotypes and more than 50 subtypes have been detected (*Kato, N.,2001*) . Each of the six main genotypes of HCV is equally divergent from one another and varies by as much as 35% of nucleic acid content, while subtypes within a typical genotype differing from each other by 20-23%. Within the infected host the viral pool comprises several different but closely related sequences called quasispecies, these may show up to 10% diversity (*Farci, P., A. Shimoda 2000*).

There is great evidence that the quasispecies nature of HCV provides a large reservoir of biologically different viral variants that may have important clinical implications for viral persistence by immune escape mechanism (*Simmonds, P., 2004*).

There is increasing evidence that patients infected with different HCV genotypes have different clinical profiles, severity of liver disease and response to alpha-interferon therapy. Hence, a convenient and reliable HCV genotyping system is essential for large-scale epidemiological and clinical studies (*Franciscus, A., 2007*).