Prevalence of hepatitis C virus among pregnant women in Egypt

Thesis

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Absract

Hepatitis C virus (HCV) infection is a major worldwide public health problem. Egypt has possibly the highest HCV prevalence worldwide. Viral hepatitis during pregnancy is associated with high risk of maternal complications. Perinatal transmission from mother to offspring is relatively low but possible (less than 10%). Our work is a cross-sectional study depending on the screening of blood samples withdrawn from (250) pregnant women in Ahmed Maher teaching hospital.

Keywords: Prevalence- Hepatitis C- pregnant- Egypt.

List of Abbreviations

AASLD	**:**	**American association for the study of liver disease**
ALT	**:**	**Alanine transaminase**
AST	**:**	**Aspartate transaminase**
CDC	**:**	**Centers for disease control and prevention**
HAART	**:**	**High activity anti-retroviral therapy**
HBV	**:**	**Hepatitis B virus**
HCC	**:**	**Hepatocellular carcinoma**
HCV	**:**	**Hepatitis C virus**
HCV-Ab's	**:**	**Hepatitis C virus antibodies**
HIV	**:**	**Human immuno deficiency virus**
IDU	**:**	**Injection drug users**
IVDu	**:**	**Intra venous drug users**
NAT	**:**	**Nucleic acid amplification testing**
PCR	**:**	**Polymerase chain reaction**
STD	**:**	**Sexually transmitted disease**
STI	**:**	**Sexually transmitted infection**
UK	**:**	**United Kingdom**
US	**:**	**United States**
WHO	**:**	**World Health Organization**
UTR	**:**	**Untranslated region**
CD81	**:**	**Cluster of differentiation 81**
NS3	**:**	**Non structural 3**
NS4	**:**	**Non structural 4**

P53	**: Protein 53**
SR	**: Super response**
SVR	**: Sustained virologic response**
RVR	**: Rapid virologic response**
E1	**: Envelope 1 protein**
EIAs	**: Enzyme Immunoassays**
ELISA	**: Enzyme linked Immunosorbant Assay**

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CHAPTER 1

Introduction

Hepatitis C virus (HCV) is one of the major etiological agents for parentrally acquired hepatitis. It is asymptomatic in large proportion of cases (65 – 75 %) and discovered accidently by abnormal liver function tests **(Farhana et al., 2009).**

The prevalence of HCV in general population ranges from 4 – 25.7%, ***(*Roy et al., 2003*)*** with highest number of infection reported in Egypt, ***(*Laurer et al., 2001*).*** The predominant HCV genotype in Egypt is genotype 4a which shows limited response to treatment **(El-Zayadi, 2002).**

The risk factors for HCV high prevalence in Nile Delta is associated with active Schistosomiases and using parenteral tarter emetic, blood transfusion, dental treatment and hospital invasive procedures **(Habib et al., 2001).**

Viral hepatitis during pregnancy is associated with high risk of maternal complications. It has been reported as the leading cause of maternal death **(Elinav et al., 2006).**

Perinatal transmission from mother to offspring is relatively low but possible (less than 10%) **(Zhou et al., 2006).**

Hepatitis C is a preventable disease with serious implications, health education and awareness of general population should be improved and screening for HCV should be encouraged **(Farhana et al., 2009).**

Aim of the Work

This study will be conducted to determine the prevalence of HCV infection among pregnant women in Ahmed Maher Teaching Hospital, Cairo, Egypt.

Hepatitis C Virus

Historical Background about HCV:

Non-A, non-B hepatitis, currently named hepatitis C virus (HCV), had been described for more than two decades, and in that time considerable advancements had been made in the mapping of routes of viral transmission**(Alter,1995).**

HCV was not explicitly identified until 1989, and blood tests were not available until 1991. This means that its emergence as a global health issue went largely undetected at the time and that analysis of the pandemic is largely retrospective. A brief history based upon currently available data is as follows:

Analysis of genetic diversity and sampling of the presence in the human population indicates that the hepatitis C virus (HCV) first infected human beings somewhere in the Far East, anything from 200 to 1500 years ago **(Simmonds, 1995).**

The viral genome was first molecularly cloned in 1988 and its organization was delineated shortly thereafter **(Bartenschlager, 2006).**

Structure of HCV:

HCV is a spherical, enveloped, single-stranded RNA virus belonging to the Flaviviridae family and Flavivirus genus. **In 2001, Lauer and Walker** reported that HCV is closely related to hepatitis G, dengue, and yellow fever viruses. HCV can produce at least 10 trillion new viral particles each day. RNA-dependent RNA polymerase, an enzyme critical in HCV replication, lacks proofreading capabilities and generates a large number of mutant viruses known as quasispecies. These represent minor molecular variations with only 1-2% nucleotide heterogeneity. HCV quasispecies pose a major challenge to immune-mediated control of HCV and may explain the variable clinical course and the difficulties in vaccine development **(Mukherjee et al,2006).**

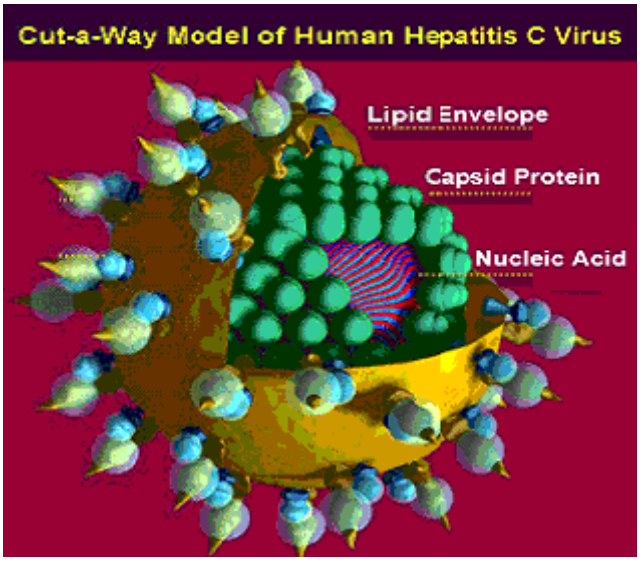

Figure 1: Cut-a-way model of Human Hepatitis C Virus
(Lauer and Walker, 2001)

The HCV genome consists of a single, open reading frame and 2 untranslated, highly conserved regions, 5'-UTR and 3'-UTR, at both ends of the genome. The genome has approximately 9500 base pairs and encodes a single polyprotein of 3011 amino acids that are processed into 10 structural and regulatory proteins.

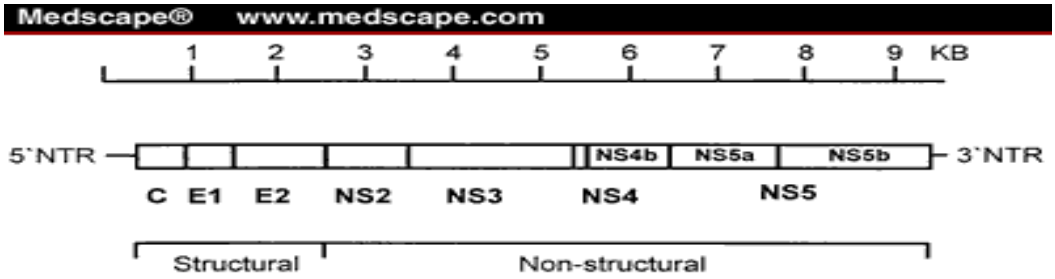

Figure 2: Hepatitis C virus genome, C, core protein; E, envelope protein; NS, nonstructural protein.

Structural components include the core and 2 envelope proteins, E1 and E2. Two regions of the E2 protein, designated hyper variable regions 1 and 2, have an extremely high rate of mutation, thought to result from selective pressure by virus-specific antibodies. The envelope protein E2 also contains the binding site for CD-81, a tetraspanin receptor expressed on hepatocytes and B lymphocytes that acts as a receptor or coreceptor for HCV.

The nonstructural components include NS2, NS3, NS4A, NS4B, NS5A, NS5B, and p7, whose proteins function as helicase-, protease-, and RNA-dependent RNA polymerase, although the exact function of p7 is unknown. One region within NS5A is linked to an interferon (IFN)

response and is called the IFN sensitivity-determining region. These enzymes are critical in viral replication and are attractive targets for future antiviral therapy. **(Mukherjee and Vinod, 2006).**

Geographical distribution of HCV genotypes:

Genotype refers to the genetic make-up of an organism or a virus. There are 6 genotypes and more than 90 subtypes of HCV, the most common in the United States being 1a and 1b (approximately 75%), 2a and 2b (approximately 15%), and 3 (approximately 7%) **(Hoofnagle, 2002).**

Type 1a and 1b are the most commonly found, they account for 65% of the worldwide isolates of HCV (**Bukh et al., 1993).** Certain genotypes such 1a, 1b, 2a, 2b, are more prevalent than others, and considerable geographical differences exist in genotype distribution (**Bukh, et al., 1995).**

El-Zayadi (2002) found that the predominant HCV genotype in Egypt is ***4a*** which shows limited response to treatment.

Hepatitis C genotype 1 is the most difficult type of HCV infection to treat successfully. Using peginterferon plus ribavirin, the current standard of care, only about 40% of HCV patients with hepatitis C experience a sustained virologic response (SVR). (**Alric,2006).**

It is well known that HCV genotypes 2 and 3 which are prevalent in North America Europe,Japan,Taiwan and parts of China, Thialand, Singapore and other parts of Southeast, patients have significantly higher sustained response rates (SVR) to treatment compared to genotypes 1 and 4 patients. Prior studies have also demonstrated that 12-14 weeks treatment is effective in genotype 2 or 3 HCV patients who become HCV undetectable after 4 weeks of therapy rapid virologic response (RVR) or "Super Responders (SR)".**(Andriulli,2005).**

Genotype 4 in Egypt and Africa, genotype 5 in South Africa, and appears to be an easy-to-treat virus with response rates similar to those of genotype 6 in Southeast Asia. The existing literature, although limited, suggests that patients with chronic hepatitis C genotypes 4-6 may exhibit different clinical courses and treatment outcomes. Ethnicity-related factors may contribute to the presence of more advanced disease in patients with genotype 4, who also tend to have a poor response to

interferon-based therapy. HCV genotype 5s 2 and 3 after a 48-week course of therapy. Response to treatment in patients with HCV genotype 6 may be at an intermediate level between that seen with genotype 1 and genotype 2 or 3. The optimal duration of treatment (24 vs 48 wk) for HCV genotype 6 is unclear and currently is under investigation**.(Nguyen and Keefe,2005)**.

Epidemiology

Prevalence and Incidence:

The estimated global prevalence of HCV infection is 2.2%, corresponding to about 130.000.000 HCV-positive persons worldwide Because many countries lack data, this estimate is based on weighted averages for regions rather than individual countries. Region-specific estimates range from < 1.0% in Northern Europe to > 2.9% in Northern Africa.The lowest prevalence (0.01%-0.1%) has been reported from countries in the United Kingdom and Scandinavia; the highest prevalence (15%-20%) has been reported from Egypt **(Shepard et al., 2005).** An estimated 27% of cirrhosis and 25% of HCC worldwide occur in HCV-infected people **(Perz et al.,2006).**

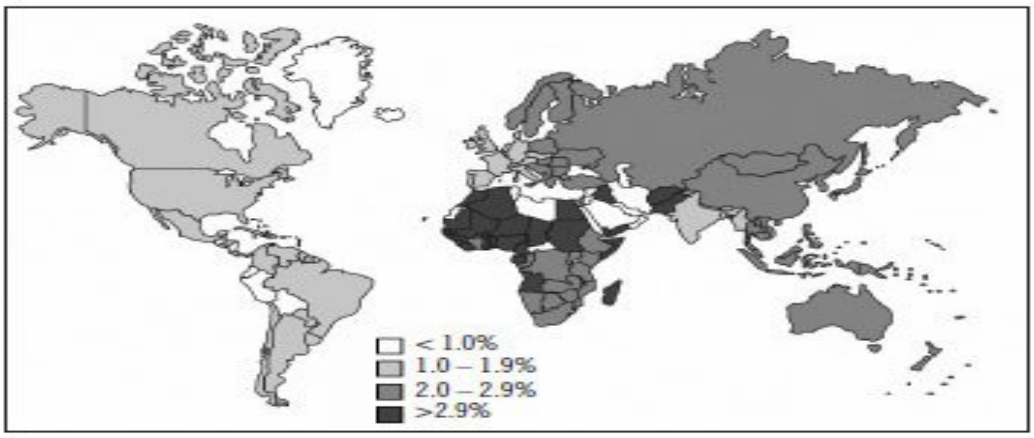

Figure 3: Estimated HCV prevalence by region.
(*Martins et al, 2011*)

There are both geographic and temporal differences in the patterns of HCV infection **(Alter et al.,2000).**

For example, vastly different countries, including the United States, Australia, Turkey, Spain, Italy, and Japan, belong to regions of the world with similar overall average prevalence of HCV infection (1.0%-1.9%), but have different patterns of age-specific prevalence (Fig.3). In the United States, prevalence is highest among persons 30-49 years old,

who account for two-thirds of all infections, and lower than average among persons less than 20 and greater than 50 years old **(Armstrong et al., 2006).**

This pattern indicates that most HCV transmission occurred in the last 20-40 years, and primarily among young adults, a pattern similar to that observed in Australia **(Law et al., 2003).**

Australia, and countries in western and northern Europe with similar HCV epidemiology **(Gerard et al., 2005*)***, the greatest variations in prevalence occur among persons with different risk factors for infection.

In contrast, the age-specific prevalences of HCV infection increase steadily with age in Turkey, Spain, Italy, Japan, and China, (Fig.3) **(Sagnelli et al., 2005).**

In these countries, persons > 50 years old account for most infections, which suggest a cohort effect in which the risk for HCV infection was higher in the distant past, i.e., 40-60 years previously. In many countries with this pattern, the greatest variations in HCV prevalence occur geographically. In Italy, Japan and China, for example, there are hyper endemic areas of the country in which older persons have an HCV prevalence 20-fold greater than the average overall and 1.5-2fold greater than the prevalence among older persons in other areas of the country **(Zhang et al., 2005).**

The highest HCV prevalence in the world occurs in Egypt, where the prevalence of infection increases steadily with age, and high rates of infection are observed among persons in all age groups (Fig.4) **(Abd El-aziz et al.,2000).**

This pattern indicates an increased risk in the distant past followed by an ongoing high risk for acquiring HCV infection, although there are regional differences in average overall prevalence **(Medhat et al., 2002).** Determining the incidence of HCV infection (i.e., the rate of newly acquired infections) is difficult because most acute infections are asymptomatic, available assays do not distinguish acute from chronic or resolved infection, and most countries do not systematically collect data on cases of acute disease. Even in countries with well-established surveillance systems, acute disease reporting systems underestimate the incidence of HCV infection **(Hagan et al., 2002).**