Introduction

Hepatitis C is a disease with a significant global impact. According to the World Organization there are 170 million people infected with the hepatitis C virus (HCV), corresponding to 3% of the world's total population. There are considerable regional differences. In some countries, e.g., Egypt, the prevalence is as high as 20%. In Africa and the Western Pacific the prevalence is significantly higher than in North America and Europe **(Wasmuth, 2009).**

Hepatitis C virus (HCV) infection in dialysis patients represents a significant health problem for dialysis units, both in term of containing the spread of infection and following the clinical progression of infected patients. Dialysis patients are a group at particularly high risk of acquiring HCV infection because of nosocomial spread. The natural history of HCV in dialysis patients remains controversial because the course of HCV typically extends over decades, while dialysis patients have higher morbidity and mortality rates than those reported in the general population limiting long-term follow-up **(Li Vecchi *et al.*, 2007).**

Liver disease due to HCV infection is a significant cause of morbidity and mortality in end-stage renal disease patients treated with dialysis or transplantation. Anti-viral therapy, after its first timed steps, is now routinely used in dialysis patients with a certain degree of liver damage and kidney transplant candidates **(Fabrizi, 2002).**

Several risk factors have been identified for HCV infection in hemodialysis patients, which include the number of blood transfusions,

the duration of hemodialysis and the prevalence of HCV infection in the dialysis unit **(Pol *et al.*, 2002).**

Nosocomial transmission of HCV in dialysis unit is considered to be an important mode of transmission of the virus **(Sanchez-Tapias, 1999).**

HCV is classified into six major genotypes. Within the genotypes there are many subtypes, with varying geographic distributions and modes of transmission **(Simmonds, 2004).**

The HCV genotype is now recognized to be the strongest predictive variable regarding to Change in Hepatitis C Virus Genotype in hemodialysis Patients response to interferon alpha (IFN) treatment. According to a recent meta-analysis the IFN-monotherapy treatment of HCV-infected hemodialysis patients with genotype 1 is associated with a sustained virological response of 30.6% (95% CI: 20.9–48%) **(Fabrizi *et al.*, 2003).**

In chronic renal failure patients, hepatitis C virus infection is often difficult to evaluate. The identification of acute HCV infection cases can be influenced by several factors: a) absence of symptoms in acute cases, the majority of them without jaundice and with symptoms related to the base of the disease or to chronic anemia; b) slight increases of aminotransferases levels; C) anti-HCV negative serology or positive after several months of contamination; and d) intermittent viremia **(Fabrizi, 2000).**

In Egypt, the prevalence of HCV infection was variable ranging from 49% to 64% from the year 1996 to 2003 It reached 52% at the

year. The prevalence of HCV infection varies greatly among various populations of patients on HD from different geographic regions. In Egypt, we found a prevalence of HCV antibodies in haemodialysis patients ranging from 52.3 to 82.3% **(Afifi *et al;* 2008).**

Aim of the work:

The aim of this study to estimate the prevalence of HCV antibodies among haemodialysis patients in Red Sea Governorate-Egypt .

Patients and methods:

All haemodiaysis patients on maintenance haemodialysis in Red Sea Governorate in Haemodialysis centers in the following cities: (Hurghada-Safaga-Ras Ghareb –Quiser- Marsa Alam- Shalateen) will be evaluated using questionnaire form including the following points :-

1	Age and Sex.
2	Cause of CKD.
3	HCV antibodies state at the start of haemodialysis .
4	Concomitant HBs antigen
5	Family history of hepatitis.
6	Timing of seroconversion .
7	Duration of haemodialysis.
8	Previous of blood transfusion.
9	Previous surgery.
10	Isolation procedures in centers. (Place isolation , Machine isolation , Staff isolation).
11	Infection control measures .
12	Switch of dialyzed patient between centers.
13	Vascular access used . 1st Vascular access :- catheter (permanent or temporary). 2nd Vascular access :- AV fistula or shunt . 3rd Vascular access :- AV graft .
14	History of Schistomiasis (Mansoni or Haematobium).

Acknowledgment

I would like to acknowledge my debt and deepest thanks to ***Prof. Dr. GAMAL ELSAYED MADY,*** *Professor Of Internal Medicine & Nephrology, Faculty Of Medicine-Ain Shams University,* who saved no time, effort or patience to guide me throughout this work. I was always supported by his expert guidance, constructive criticism and wise counsel throughout this work.

My deepest gratitude and appreciation are expressed to ***Dr. WALEED ANWAR ABDELMOHSEN,*** *Lecturer of internal Medicine & Nephrology, Faculty of Medicine, Ain Shams University,* for his generous help and valuable comments during every step in the preparation of this work.

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Prevalence of Antibodies to Hepatitis-C Virus Infection Among Haemodialysis Patients in Red Sea Governorate/Egypt

Thesis

Submitted for partial fulfillment of master degree in

NEPHROLOGY

BY

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2013

نسبة وجود الأجسام المضادة لعدوى الالتهاب الكبدى الفيروسى سى بين مرضى الاستصفاء الدموى فى محافظة البحر الاحمر جمهورية مصر العربية

رسالة علمية
توطئة للحصول علي درجة الماجستير في امراض الكلى

مقدم من
الطبيب/ باسم يوسف صديق
بكالوريوس الطب والجراحة – جامعة أسيوط

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(2013)

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HCV Background

The hepatitis C virus (HCV) belongs to the Flaviviridae family and is the only member of the Hepacivirus genus. HCV infection is a major cause of chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma (HCC) worldwide **(National Institutes of Health Consensus Development Conference, 2002).**

Epidemiology:

Hepatitis C is a disease with a significant global impact. According to the World Health Organization there are 170 million people infected with the hepatitis C virus (HCV), corresponding to 3% of the world's total population. There are considerable regional differences. In some countries, e.g., Egypt, the prevalence is as high as 20%.In Africa and the Western Pacific the prevalence is significantly higher than in North America and Europe **(Wasmuth, 2009).**

It is estimated that there are 2-5 million HCV-positive persons in Europe. The prevalence of HCV-antibodies in otherwise healthy blood donors is approximately 1.6%in the United States, 1.15% in Italy, 0.4% in Germany, and 0.23% in Scandinavia**(Anonymous, 2004**).

The number of patients actually HCV RNA positive is estimated to be around 80 to 90% of all HCV-antibody positive persons. Certain groups are preferentially affected: The highest risk factor in most instances is injection drug use. But patients undergoing hemodialysis and persons who received blood transfusions before 1991 are at risk also. In Europe and the United States chronic hepatitis C is the most

common chronic liver disease. The majority of liver transplants performed in these regions are for chronic HCV.It is difficult to determine the number of new HCV infections, as most acute cases will not be noticed clinically. Fewer than 25% of acute cases of hepatitis C are clinically apparent. In addition, the age of infection upon diagnosis is not possible to determine in most cases. Nevertheless, it has to be assumed that the number of new infections has considerably decreased over the past decades. For the United States it is estimated that the number of new cases of acute HCV infection has fallen from approximately 230,000 per year in the 1980s to about 20,000 cases per year currently **(Wasley, 2008)**.

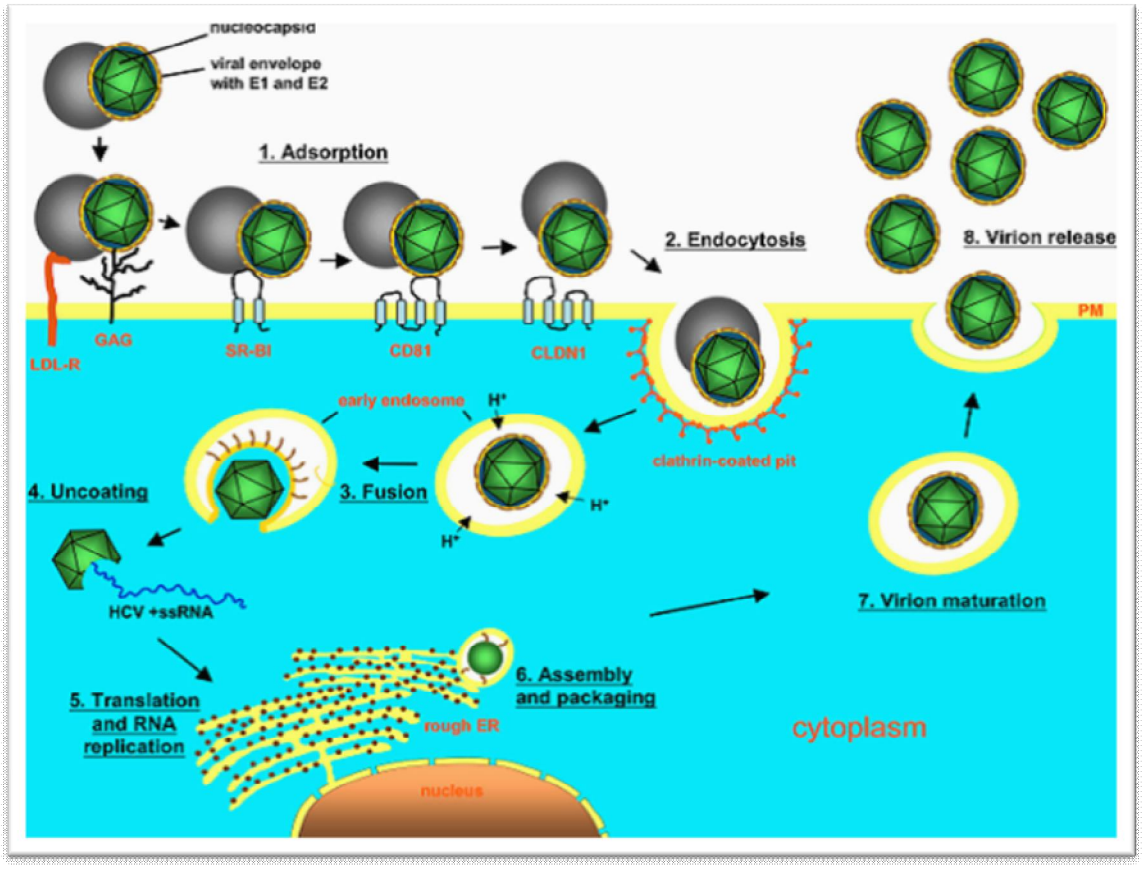

Fig.(1-1): Current model of the HCV lifecycle **(Kupfer, 2009).**

Surrogate models for the study of the early steps of viral life cycle have been established, including infectious retroviral pseudotypes displaying functional HCV glycoproteins. These pseudotypes turned out to provide a robust model system for the study of viral entry **(BartoschB et al., 2003)**.

Structure of the HCV genome :

In 1989 the HCV was cloned and identified as the major cause of parentally transmitted non-A, non-B hepatits (NANBH). HCV is a flavivirus composed of a 10 kb single positive strand RNA. The viral genome encodes a precursor polyprotein of about 3000 amino acids, co- and post-transcriptional cleavages of which generate the core, seven non-structural (p7, NS2-5) proteins and two glycoproteins which constitute the envelope proteins E1 and E2 (non-coding region (5'NCR) represents the most conserved one **(Fehr et al., 2004, Houghton et al., 1991).**

Several HCV genotypes have been identified and significant genetic heterogeneity has been observed over the entire viral genome. The regions encoding the E1 and E2 are the most variable sequences of the viral genome, while the 5' non-coding region (5'NCR) represents the most conserved one *(Figure1-2).*

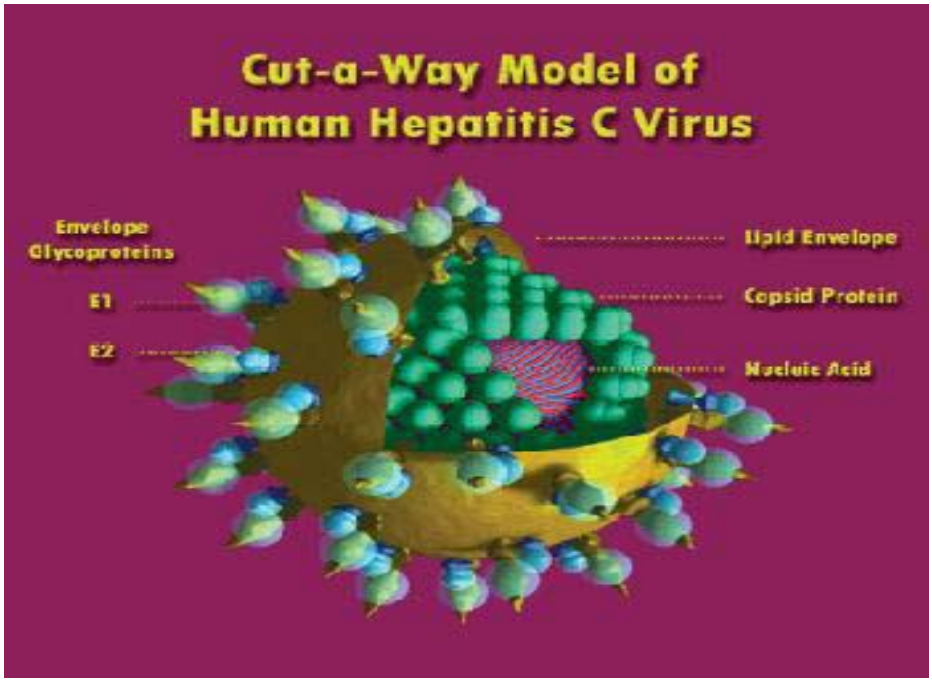

Figure (1-2): Cut-a-way model of HCV with the presentation of lipid envelope, envelope glycoprotein (E1 and E2) and nucleotides

Viral heterogeneity:

The polymerase enzyme of RNA viruses such as HCV, lacks proof-reading ability and is therefore unable to correct copying errors made during viral replication. Many of these nucleotide changes result in a nonfunctional genome or a replication incompetent virus (lethal mutants). However, others persist and account for the tremendous viral diversity that is characteristic of HCV**(Chopra, 2009).**

This heterogeneity is extremely important in the diagnosis of infection, pathogenesis of disease, and the response to treatment; it prevents the development of conventional vaccines, allows the virus to escape eradication by the host's immune system, and affects the completeness of the response to antiviral therapies such as interferon.

Viral heterogeneity takes several forms depending upon the degree of diversity. QuasI-species are families of different, but highly similar, strains that develop within an infected host over time. Nucleotide sequence homology is greater than 95 percent**(Chopra, 2009).**

Genotypes :

Six major genotypes of HCV have been defined. More than 50 subtypes have also been described; the most common subtypes are 1a, 1b, 2a, and 2b. The evolution of genotypes has probably been influenced by several factors, including immune selection, infection patterns, replication efficiency, and population migration. So, there is a distinct geographic distribution of HCV genotypes:

- Genotype 1&2 is most common in the UnitedStates and Europe.
- Genotype 3 is most common in India, the Far East, and Australia.
- Genotype 4 is most common in Africa and the Middle East
- Genotype 5 is most common in South Africa.
- Genotype 6 is most common in HongKong ,Vietnamand, Australia.

(Chopra, 2009).

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 percent with genotype 1 (including 1a and 1b) to as high as 70 to 80 percent with genotypes 2 and 3**(Chopra, 2009).**