

**Prevalence of HCV Antibodies in
haemodialysis patients in El-
Beheira governate (Sector A)**

Thesis

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degree in internal medicine*

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وَسَيُجَنَّبُكَ الَّذِينَ اتَّخَذُوا مِن دُونِ اللَّهِ آلِهَةً مِّثْلَكَ
(وَعَلَّمَكَ مَا لَمْ تَكُن تَعْلَمُ وَكَانَ فَضْلُ اللَّهِ
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List Of Abbreviations

<i>AAMI</i>	American National Standards Institute
<i>ALT</i>	Alanine aminotransferase
<i>AN69</i>	Poly acryl nitrile
<i>AST</i>	Aspartate aminotransferase
<i>CAH</i>	Chronic active hepatitis
<i>CDC</i>	Centers for Disease Control and Prevention
<i>CKD</i>	Chronic kidney disease
<i>CSN</i>	Canadian Society of Nephrology
<i>CU</i>	cuprophane membrane
<i>DNA</i>	deoxyribonucleic acid
<i>DOPPS</i>	Dialysis Outcomes and Practice Patterns Study
<i>EIA</i>	Enzyme Immuno Assay
<i>ELISA</i>	Enzyme Linked Immunosorbent Assay
<i>EM</i>	electron microscopy
<i>EOT</i>	end-of-therapy
<i>EPA</i>	U.S. Environmental Protection Agency.
<i>EPO</i>	Erythropoietin
<i>ESRD</i>	End-stage renal disease
<i>ETR</i>	end of treatment response
<i>EVR</i>	early virologic response
<i>FDA</i>	U.S. Food and Drug Administration.
<i>FSGS</i>	focal segmental glomerulosclerosis
<i>GN</i>	Glomerulonephritis
<i>HBsAg</i>	Hepatitis B surface antigen
<i>HBV</i>	Hepatitis B virus
<i>HCC</i>	Hepatocellular Carcinoma
<i>HCcAg</i>	Hepatitis C core antigen

HCV	Hepatitis C virus
HCV RNA	Hepatitis C virus ribonucleic acid.
HD	heamodialysis
HGF	hepatocyte growth factor
HIV	Human immunodeficiency virus
HVR	Hyper Variable Region
IFN	interferon
IgA	immunoglobulinA
IgG	immunoglobulin G
IL	interleukin
IV	Intravenous
IVDA	Intravenous drug abuse
KDIGO	Kidney Disease: Improving Global Outcomes
LFTs	liver function tests
LM	light microscopy
MHD	maintenance heamodialysis
MICS	Malnutrition–inflammation complex syndrome
MN	membranous nephropathy
MPGN	Membranoproliferative glomerulonephritis
NAT	Nucleic acid test(ing)
NHL	non Hodgkin’s lymphoma
ORF	Open Reading Frame
PCR	Polymerase chain reaction
PD	peritoneal dialysis
PEGIFN	Pegylated IFN
PPE	personal protective equipment
PS	polysulfone membrane
PTDM	post transplant diabetes mellitus
RF	rheumatoid factor

<i>RIBA</i>	Recombinant immunoblot assay.
<i>RT.</i>	Renal transplantation
<i>RT-PCR</i>	Reverse transcriptase polymerase chain reaction
<i>SS</i>	Sjogren syndrome
<i>SVR</i>	Sustained virologic response
<i>TFG</i>	Transforming growth factor
<i>TMA</i>	Transcription-mediated amplification

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Introduction

Hepatitis C is the most common cause of chronic viral liver disease in haemodialysis patients(**Hinrichsen H et al.,2002**) Hemodialysis (HD) patients have an increased risk of exposure to hepatitis C virus (HCV). The relevance of HCV infection in HD patients is due to the documented increased risk of death due to chronic liver disease in these patients, particularly after kidney transplantatio (**Nemati E et al.,2009**) .

The natural course of hepatitis C in haemodialysis patients is not well understood. It seems to differ from that in other HCV patients(**Simon N et al.,1994**).Liver function tests are close to or near normal in many case (**Guh JY et al.1995**)But the mortality of HCV infected haemodialysis patients seems to be enhanced compared with HCV negative haemodialysis patients in preliminary studies(**Stehman-Breen CO et al.1998**). Thus patients with HCV on chronic haemodialysis are at increased risk of death, which suggests that the focus should be directed more to identification and prevention of hepatitis C

infection in haemodialysis patients.

The prevalence of HCV infection among HD patients varies from country to country and from one center to another. The reported prevalence of HCV infection among dialysis patients in developed countries ranges from 3.6 to 20%; (**Jadoul M** et al.,2004). it is much higher in developing countries (**jaiswal SK et al.,2002**). The prevalence of anti-HCV among dialysis patients was 0.4% in the 8.4% in the United States (2000)(**Tokars JI et al.,2002**). 43.9% in Saudi Arabia (2001), 30% in India (2002), and 41% in Turkey (2001).

Several risk factors are suggested to be related to HCV dissemination in HD centers. Repeated blood transfusions, shared dialysis machines, surgery, nosocomial route and multi-dose drug vials are the major suggested routes for spread of HCV infection in HD unit (**Nobakht Haghighi A** et al.,2001). Partial immunosuppression found in HD patients, resulting in a poor antibody response, may play a role in sensitizing them to acquire the infection through uncommon ways.

The extensive use of recombinant erythropoietin to correct renal anemia in haemodialysis patients resulted in a significant reduction in blood transfusions. However, previous studies have shown that de novo infections in single haemodialysis units may still occur in the absence of other parenteral risk factors (**Fabrizi F et al.,1998**).

In recent years, HCV viraemia (HCV-RNA) has been routinely detected by polymerase chain reaction (PCR) (**Gretch D et al.,1995**). In 1993, Bukh and colleagues were the first to describe the fact that HCV viraemia can occur without detection of HCV antibodies. This has been confirmed by several authors in small patient populations(**Seeling R et al.,1994**). Most epidemiological studies in haemodialysis patients have been performed using serological testing of hepatitis C antibodies only(**Fabrizi F et al.,1993**). Several prevalence studies of hepatitis C have been undertaken. There is a wide range in HCV antibody positivity and HCV viraemia within the studies, ranging from 1% up to 91%.

Aim of the work

This work aims to assess the size of HCV problems in Haemodialysed patients in El-Beheira governate (sector A) as regards mode of transmission, prevalence, detection, prevention & treatment.

Also this work aims to predict the factors that share in increasing the incidence of this problem and to give the recommendations for preventing transmission of HCV infection.

Epidemiology of HCV

The estimated global prevalence of HCV infection is 3%, corresponding to about 170 000 000-200 000 000 HCV-positive persons worldwide (**Castera et al.,2006**). 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**).

The natural history of HCV infection in the general population after 15-20 years evolution (from transmission) are as follow:

(1)Chronic active hepatitis (CAH) is observed in ~60%of cases.(2)Overt liver cirrhosis will develop in ~30% of CAH subgroup,giving an overall figure of ~18%.

(3) Liver cancer will be the ultimate consequence in ~15% of cirrhosis subgroup with an overall figure of 2-3% in infected individuals (**Berthoux et al., 2000**)

In recent years, after the identification of hepatitis C virus (HCV) in 1989(**Choo et al., 1989**) and the introduction of diagnostic tests

which able to detect antibodies against HCV. The prevalence of anti-HCV antibodies in maintenance hemodialysis patients varies widely from country to country and center to center, with reported rates ranging from 0 to 95% (**Huang, 2002**)

Therefore, hepatitis C virus (HCV) infection is the most common cause of chronic liver disease in hemodialysis patients (**Espinosa et al., 2001**)

Hepatitis C virology

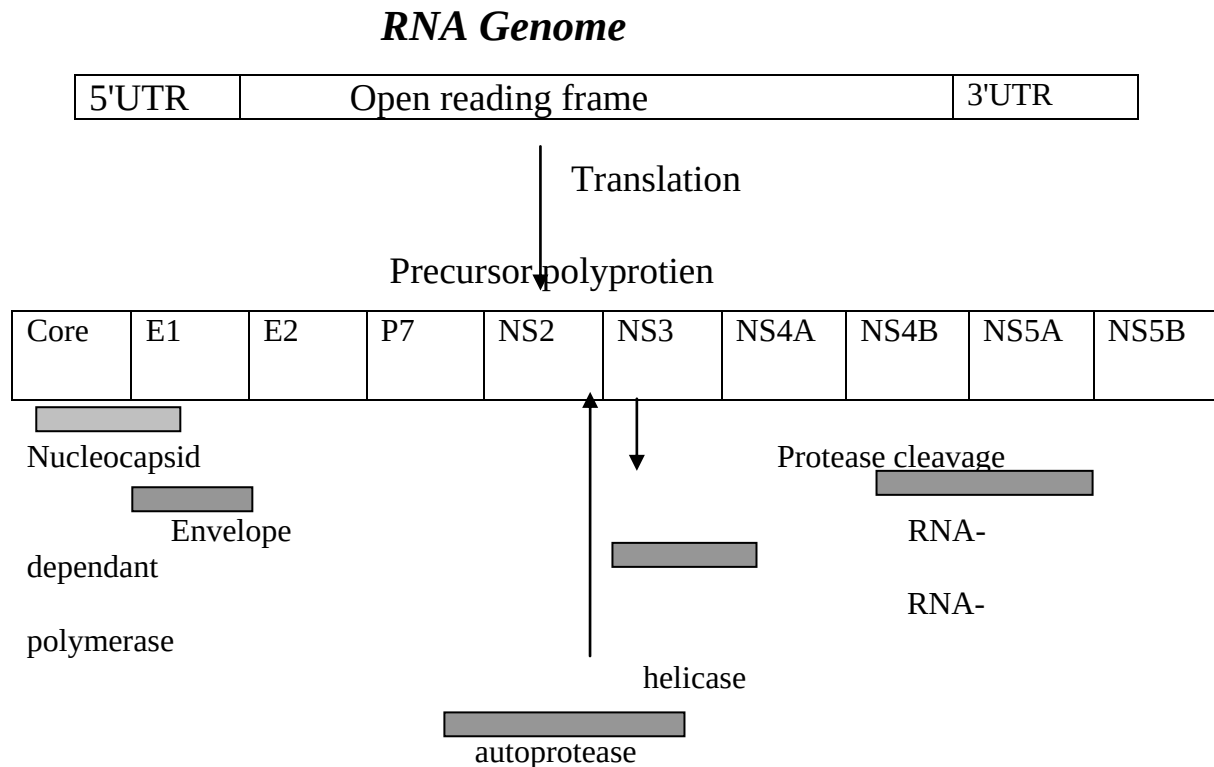
It became apparent after the discovery of the hepatitis A and B viruses in the late 1960s and early 1970s that a large proportion of cases of acute and chronic hepatitis could not be explained by either of these agents. Another viral agent were said to have non-A non –B hepatitis. The agent was finally 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 structure of hepatitis c:

Hepatitis C virus is a member of the Flaviviridae family. It comprises appositive –single stranded RNA molecule of about 9,400 nucleotides in length. It contains along translational open reading frame (ORF) that encodes a large viral polypeptide of 3011 amino acids. ORF is translated to yield a polyphonies from which viral proteins derived by

post-translational cleavage to yield structural (core and envelop) and non structural (ns) proteins (**Figure1**)(**Lauer and Walker,2001**).

Figure 1. the HCV Genome and expressed polyphonies (**Lauer and Walker .,2001**)



The genome contains highly conserved untranslated regions (UTR) at both 5' and 3' termini, which flank of large translation open reading frame(ORF).The structural region contains the nucleocapsid core protein and two envelope proteins (E1 and E2) that are located in the N-terminal quarter ,while the non-structural proteins ,(NS2,NS3,NS4A,NS4B,NS5A and NS5B)is in the remaining portion of the polyphonies (**Lauer and Walker.,2001**)