Prevalence of HCV Antibodies in hemodialysis patients in Luxor governorate

Thesis

Submitted for partial fulfillment of master degree in nephrology

BY

Ahmed Abdel Galil Helmy

(M.B.B.Ch.)

Under supervision of

Prof .Dr. MOHAMED EL - TAYEB NASSER

Prof. of internal medicine&nephrology

Ain shams university

Dr.ABER HALIM BAKI

Lecturer of internal medicine&nephrology

Ain shams university

Faculty of medicine
Ain shams university
Cairo 2013

بسم الله الرحمن الرحيم

(قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْحَكِيمُ)

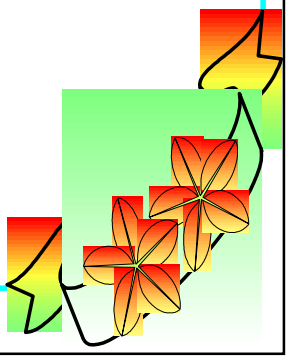
(سورة البقرة:٣٢)

Dedication

My work is dedicated to:

My dear Family.

Ahmed Abdel Galil



Acknowledgement

First thanks to ***ALLAH*** *to whom I relate any success in achieving any work in my life.*

I wish to express my deepest thanks, gratitude and appreciation to ***Prof. Dr. MOHAMED EL - TAYEB NASSER,*** *Professor of Internal Medicine and Nephrology, Faculty of Medicine- Ain Shams University for his meticulous supervision, for his kind guidance, valuable instructions and generous help.*

Special thanks are due to ***Dr. Aber Halim Baky,*** *Lecturer of internal medicine and nephrology ,Faculty of Medicine- Ain Shams University for his sincere efforts, fruitful encouragement.*

My deepest thanks are also to ***Prof. Dr. Mostafa El-Hosini*** *Professor of Community, Environmental and Occupational Medicine, Faculty of Medicine- Ain Shams University for his kind help during the practical part of the work.*

Lastly, I want to thank all my staff, my family, my colleagues and my patients without their help this work could not have been completed.

Ahmed Abdel Galil

List of Contents

Title Page No.

Introduction ***.....1***

Aim of the work ***.....4***

Review of Literature

- *Hepatitis C virus (HCV) Infection* ***.....5***
- *HCV Infection in Hemodialysis* ***.....27***
- *HCV Infection in Hemodialysis in Egypt* ***.....58***

Patients and Methods ***.....62***

Results ***.....64***

Discussion ***.....75***

Summary ***.....86***

Conclusion ***.....89***

Recommendation ***.....90***

References ***.....91***

Arabic Summary

List of Figures

Fig. No. Title Page No.

Fig. (1): Hepatitis C infection in the US by source……...8

Fig. (2): Serologic results in cases of acute HCV that do not progress to chronic infection and in cases of chronic HCV…...13

Fig. (3): Natural history of HCV infection……14

Fig. (4): Testing algorithm for HCV infection in asymptomatic patients……..……...16

Fig. (5): Treatment algorithm for chronic HCV infection……..... 20

Fig. (6): Hepatitis C virus in Egypt compared to other countries in the world…… ….23

Fig. (7): Showing age of the studied group ……....64

Fig. (8): Showing gender of the studied group……....65

Fig. (9): Causes of renal failure in the studied group……....66

Fig. (10): Showing prevalence of HCV among Dialysis Patients at the start of hemodiaysis in the studied group……..……...67

Fig. (11): Showing sero-convertion status of HCV among the studied group……...68

List of Tables

Table No.	Title	Page No.
Table (1):	Contraindications to Treatment of HCV Infection with Interferon Plus Ribavirin	18
Table (2):	Hepatitis C prevalence among Asian HD patients	30
Table (3):	Hepatitis C prevalence among US and European HD patients	31
Table (4):	Hepatitis C prevalence among African and non-US American HD patients	32
Table (5):	Brief details of studies showing benefit of isolation of HCV patients in HD units	53
Table (6):	Comparison of different guidelines on HCV during maintenance hemodialysis	55
Table (7):	Prevalence of HCV infection in hemodialysis patients from various countries	59
Table (8):	Annual reports of Egyptian registry from 1996 to 2008	60
Table (9):	Descriptive Analysis of age of the studied group	64
Table (10):	Descriptive Analysis of gender of the studied group	65
Table (11):	Causes of renal failure in the studied group	66
Table (12):	Shows the classification of patients according to their viral status at the start of HD	67
Table (13):	Prevalence of HCV among Dialysis Patients	68
Table (14):	Descriptive Analysis showing comparison between HCV seroconverted and free cases regarding age and duration of the Dialysis (by years)	69
Table (15):	The univariate analysis of the factors affecting the HCV seroconversion	74

List of Abbreviations

ALT	*Alanine Aminotransferases*
AST	*Aspartate Aminotransferases*
BSI	*Rates of Bloodstream Infections)*
CDC	*Center for Diseases Control and Prevention*
CKD	*Chronic kidney disease*
CVC	*central venous catheter*
DOPPS	*Dialysis outcomes and practice patterns study*
EIA	*Enzyme Immune Assay*
ELISA	*Enzyme Linked Immunosorbent Assay*
ESRD	*End stage renal disease*
FDA	*Food and Drug Administration*
HCV	*Hepatitis C Virus*
HD	*Hemodialysis*
HIV	*Human Immunodeficiency Virus*
IRES	*Internal ribosomal entry site*
KDIGO	*Kidney Disease Improving Global Outcome*
NCR	*Non coding region*
NIH	*National Institute of Health*
ORF	*Open reading frame*
PA	*Physician Assistant*
PCR	*Polymerase Chain Reaction*
RCT	*Randomized controlled trial*
RIBA	*Recombinant Immunoblot Assay*
SVR	*Sustained viral response*
TMA	*Transcription mediated amplification*

Introduction

Hepatitis C virus (HCV) infection, first identified in 1989, is caused by a blood- borne virus and affects an estimated 120 million individuals worldwide. Almost 75% of HCV infections become chronic ***(Zuure et al., 2010).***

Hepatitis C virus (HCV) infection is gaining increasing attention as a global health crisis. Egypt reports the highest prevalence of HCV worldwide, ranging from 6% to more than 40% among regions and demographic groups. ***(Lehman EM, Wilson M L.,2009)*** .

The prevalence positive for antibody to HCV was 14.7%. . The issue of treatment for those that develop HCV related liver disease is essentially a medical care crisis for the country***.(EDHS. 2009).***

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 2008 ***(Egyptian renal registry ., 2008 report) .***

The prevalence of anti-HCV antibodies in serum among hemodialysis (HD) patients is consistently higher than in the general population, indicating an increased risk of acquiring HCV infection among HD patients ***(Jasuja et al., 2009).***

Hepatitis C virus (HCV) infection is a significant cause of morbidity and mortality in haemodialysis (HD) patients. The reported prevalence of HCV among the HD population has varied greatly from 1.9 to 84.6% in

different countries in recent years. The length of time on HD is generally believed to be associated with HCV acquisition in HD subjects. ***(Mohammad Rahnavardi, et al., 2008).***

The prevalence of HCV was found to be significantly increased in the older age group, duration on dialysis , number of blood transfusions. ***(Kim 2002)*** ,nosocomial transmission within HD units ***(Fambrizi et al.,2002)*** ,among men than among women ***(Sypsa et al.,2005)*** ,coinfection with HBV**.** ***(Santos et al.,2007***) and diabetic nephropathy was found to be a more frequent cause of ESRD among the anti-HCV antibody-positive patients ***(Iwasa et al.,2008).***

Evaluating the natural history of HCV among HD patients faces great controversy because the onset is rarely over recognized, the course of HCV is usually indolent and extends decades rather than years, and HD patients may actualy die from various comorbid conditions before the long-term consequences of HCV infection have been established**.*(Rahnavardi M et al.,2008).***

Haemodialysis (HD) patients are at high risk of infection by hepatitis C virus. Such factors as blood transfusion, immunosuppressant, and frequent parenteral interventions have been associated with an increased risk for infection. At present, nosocomial transmission within the dialysis centres, through contamination of the hands of the staff members or of items shared between patients, appears to be the principal route of HCV spreading in this population. Mode of dialysis, number of blood transfusions, HCV prevalence in the respective unit and history of intravenous drug use have being also implicated. An early and accurate

HCV diagnosis in end-stage renal disease patients is important for the prevention of transmission as well as the appropriate management of the infection***.(Makhlough A et al.,2008).***

The higher prevalence in developing countries in comparison with developed countries reflects many factors including socioeconomic factors, bad infection control measures, the use of blood transfusion instead of Erythropoietin to treat anemia and the higher prevalence of HCV infection among the general population in developing countries. ***(Afifi et al., 2009).***

Aim Of The Work

The aim of this multicenter study is to retrospectively investigate the HCV seroconversion and prevalence of hepatitis C virus (HCV) infection among all hemodialysis patients in Luxor governerate and delineate events and factors associated with HCV seroconversion.

Hepatitis C virus (HCV) infection;

The hepatitis C virus (HCV) is a major cause of liver disease world wide and will be a potential source of substantial cases of morbidity and mortality in the future ***(Shepard et al .,2005).*** It is estimated that approximately 130-210 million individuals, i.e. 3% of the world's population, are chronically infected with the HCV ***(Lavanchy2009).***

Prevalence;

The prevalence varies markedly from one geographical area to another and within the population assessed ***(EASL 2011).***

In Western Europe, HCV prevalence rates range from 0.4% to 3%. It is higher in Eastern Europe and the Middle East, in countries such as Egypt (15%), Romania (6%), Pakistan (4.7%) and in Ukraine (4.0%) ***(Negro and Alberti .,2011).***

There is a wide range of prevalence estimates among developing countries, and generally less data available to validate assumptions about the burden of disease, than in the developed world ***(Sievert et al .,2011).***

HCV structure;

HCV is a positive strand RNA virus of approximately 9.6 Kb in length. Its genome is composed of a 5' non-coding region (5'NCR), a long open reading frame (ORF) encoding a polyprotein precursor of about 3,000 amino acids and 3'NCR. The 5'NCR functions as internal ribosomal entry site (IRES) essential for cap independent translation of the viral RNA ***(Bartenschlage et al., 2004)***.

The core region has numerous functional activities. These include its role in encapsulation of viral RNA, a regulatory effect on cellular and viral promoters, interactions with a number of cellular proteins, a modulator role in cell death under certain conditions, involvement in cell growth promotion and immortalization, induction of HCC in transgenic mice and a possible immuno-regulatory role ***(Ray and Ray, 2001)***.

HCV Genotypes;

The hepatitis C virus belongs to the genus Hepacivirus a member of the family Flaviviridae. Until recently it was considered to be the only member of this genus. However a member of this genus has been discovered in dogs - canine hepacivirus.***(Kapoor et al 2011)***. There is also at least one virus in this genus that infects horses***(Burbelo et al., 2012).***

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 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). Accumulation of nucleotide substitution in the HCV genome results in diversification and evolution into different genotypes and subtypes. No fewer than 6 genotypes and more than 50 subtypes have been detected ***(Kato, 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 ***(Omran et al., 2009).***

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 epidemio-logical and clinical studies ***(Franciscus, 2007)***.

Transmission;

The hepatitis C virus is transmitted by blood-to-blood contact. In developed countries, it is estimated that 90% of persons with chronic HCV infection were infected through transfusion of unscreened blood or blood products or via injecting drug use or sexual exposure. In developing countries, the primary sources of HCV infection are unsterilized injection equipment and infusion of inadequately screened blood and blood products. There has not been a documented transfusion-related case of hepatitis C in the United States for over a decade, as the blood supply is vigorously screened with both ELIZA and Polymerase chain reaction (PCR) technologies ***(Tohme and Holmberg, 2010).***

Parenteral exposure to the hepatitis C virus is the most efficient means of transmission. Accordingly, the majority of patients infected with HCV in Europe and the United States acquired the disease through intravenous drug use or blood transfusion. The latter has become rare since routine testing of the blood supply for HCV began in the early 1990s. Other types of parenteral exposure are important in specific regions in the world ***(Stramer et al., 2004).***