Transient Elastography to Assess Hepatic Fibrosis in Chronic Hemodialysis Hepatitis C Patients At Kasr Al Ainy Hospital.

Thesis
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Abstract

AIM: To assess liver fibrosis in chronic hepatitis C hemodialysis patients by fibroscan and comparing its results with serum hyaluronic acid level.

Method: This is cross sectional study was conducted from July 2012 to March 2014 on a cohort of 134 Egyptian patients on chronic hemodialysis patients at Kasr Al Ainy hospital (King Fahd and Kidney & dialysis units) aged between 17 and 67 years for more than one year of hemodialysis. All patients were subjected to routine labs, HBs Ag, HBc Ab, HBe Ag, HCV Ab and HIV Ab, quantitative PCR for both HCV and HBV, hyaluronic acid serum level, alpha feto protein (AFP). Abdominal ultrasound was done to positive cases, 29 patients out of 77 HCV positive patients had a fibroscan done and results are correlated with serum hyaluronic acid level.

Results: The mean of age is 47.43 ± 12.65 years, 50.7 % males and 49.3% female, duration range was 1-18 with mean 5.96 ± 4.12 years. The most common cause for ESRD was hypertensive nephropathy 32.1% and diabetic nephropathy 18.7%. HCV +ve 57.5 % and 42.5% -ve, HBV +ve 3%.There was significant correlation between HCV PCR and duration of hemodialysis ($p < 0.001$), number of blood transfusions ($p < 0.001$) and hyaluronic acid (p 0.029). Significant correlation between serum hyaluronic acid and hemodialysis duration (p 0.003). Significant correlation between serum hyaluronic acid and fibroscan ($p < 0.001$).

Conclusion: Fibroscan is a simple non invasive test that can be used to assess liver fibrosis in hemodialysis patients.

Key Words: CHC, Hemodialysis, Transient elastography (TE, Fibroscan), Hyaluronic acid.

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ABBREVIATIONS:

AASLD …..American Association for The study of Liver diseases

ALT….. Alanine Aminotransferase

AST….. Aspartate Aminotransferase

CDC….. Centers for Disease Control and Prevention

CHC ….. Chronic Hepatitis C

CKD….. Chronic Kidney Disease

DCs…..Dendritic cells

DM…..Diabetes Mellitus

DN…..Diabetic Nephropathy

EIA ….. Enzyme Immunoassay

ESRD…..End Stage Renal Disease

ESRF….. End Stage Renal Failure

FDA….. Food and Drug Administration

FSGS…..Focal Segmental Glomerulosclerosis

GFR…..Glomerular Filteration Rate

HA….. Hyaluronic Acid

HBV….. Hepatitis B Virus

HCC…..Hepatocellular Carinoma

HCV ….. Hepatitis C virus

HD…..Hemodialysis

HIV….. Human Immunodeficiency Virus

IDSA….. Infectious Diseases Society of America

IFN…..Interferon

INR….. International Normalized Ratio

IQR ….. Interquartile Range

IR…..Insulin resistence

KDIGO….. Kidney Disease: Improving Global Outcomes

KDOQI….. Kidney Disease Outcomes Quality Initiative

LCM…..Laser Capture Microdissection

LSM…..Liver Stiffness Measurement

MMP….. Matrix Metalloproteinase

MPGN…..Membranoproliferative Glomerulonephritis

NAT…..Nucleic Acid Testing

PCR ….. Polymerase Chain Reaction

PD…..Peritoneal Dialysis

PLB ….. Percutaneous liver biopsy

ROC curve…..Receiver Operator characteristic curve

SLE…..Systemic Lupus Erythematosis

TE…..Transient Elastography

USRDS….. US Renal Data System

WHO….. World Health Organization

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Introduction

In clinical practice, assessing hepatic fibrosis for hemodialysis patients with chronic hepatitis C (CHC) can help to evaluate the eligibility for renal transplantation, the necessity for IFN-based therapy, the longterm prognosis, and complications related to portal hypertension and hepatocellular carcinoma (**Fabrizi et al,2008)**.

Although percutaneous liver biopsy (PLB) is the gold standard for staging hepatic fibrosis in hemodialysis patients with chronic hepatitis C (CHC) before renal transplantation or antiviral therapy, concerns exist about serious post biopsy complications (**Kaw and Malhotra ,2006)**.

Using transient elastography (TE,Fibroscan) to predict the severity of hepatic fibrosis has not been prospectively evaluated in these patients.

This study will be based on the results of a previous study by ***Liu et al, (2011)*** who concluded that TE is superior to APRI in assessing the severity of hepatic fibrosis and can substantially decrease the need of staging PLB in hemodialysis patients with CHC.

Aim of Work

The aim of this study is to Evaluate the efficacy of elastography in the diagnosis of hepatic fibrosis among chronic HCV hemodialysis patients.

Chapter 1
Hepatitis C in Egypt

The World Health Organization has declared hepatitis C a global health problem, with approximately 3% , or around 170 million persons of the world's population infected with HCV ***(World Health Organization 2004)*** and ***(Shepard CW et al., 2005)***.

Egypt has the highest prevalence of hepatitis C in the world ***(Lavanchy D , 2011)***. The national prevalence rate of HCV antibody positivity has been estimated to be between 10-13%, since 30-40% of individuals clear the infection shortly after exposure based on national studies and village studies in Egypt, the estimated adjusted national prevalence rate of chronic hepatitis C infection is 7.8% or 5.3million people in 2004. Only one third of these individuals (1.75 million) are estimated to have chronic liver disease (elevated ALT) and, furthermore, among these one third (577,000 people) are suffering from advanced liver disease ***(Mohamed MK. 2004)***.

Hepatitis C virus genotype 4 (HCV-4) (mostly 4a) is the most common variant of the hepatitis C virus (HCV) in the Middle East and Africa, particularly Egypt ***(Kamal SM et al., 2008) and (Egyptian Ministry of Health 2007)***. Genotype 4 represents over 90% of cases in Egypt ***(Abdel-Aziz F et al., 2000)***. Chronic HCV is the main cause of chronic hepatitis, liver cirrhosis, hepatocellular carcinoma and liver transplantation in Egypt and, indeed, one of the top five leading causes of death ***(Nguyen MH et al., 2005)***.

Hepatitis C virus in Egypt compared to other countries in the world is shown below in the graph.

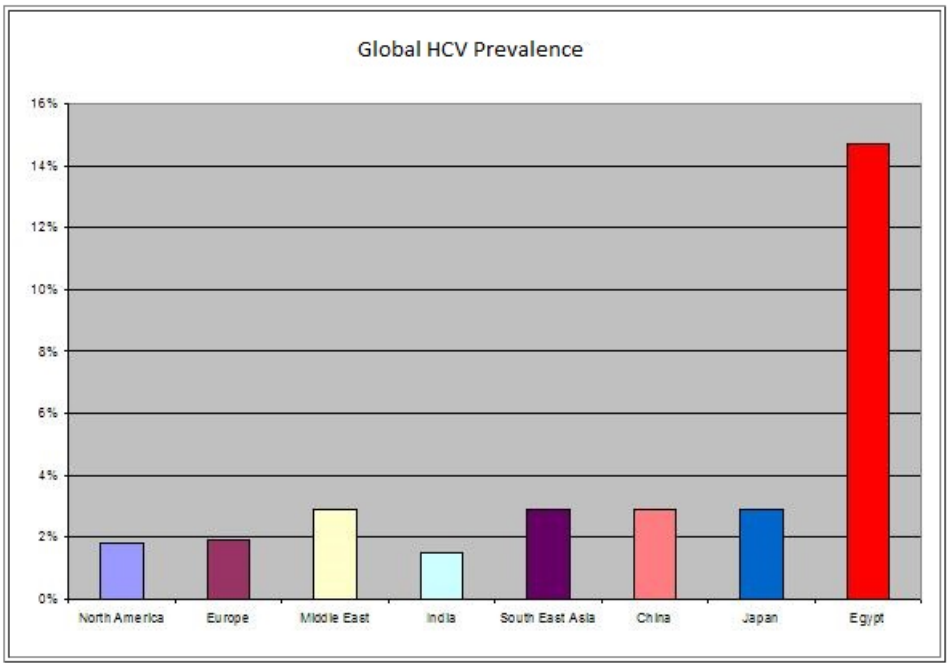

Fig (1) The currect population in Egypt is about 78 to 80 million. 14.7% of this popuation who have been infected with this virus. This number is an underestimate becasue it does not include the number of people who have been infected that are under 15 years of age or over 60 years of age. Not everyone remains infected but EDHS reported that 9.8% continue to have HCV RNA. That means almost 10% of the total population are infected and are infectious to other people. That is 7.8 million people with chronic active HCV infection. This also is an underestimate becasue it does not include the number of people who have been infected that are under 15 years of age or over 60 years of age that are chronically infected. The issue of treatment for those that develop HCV related liver disease is essentially a medical care crisis for the country. **(El-Zanaty F et al., 2009).**

Prevelance of HCV in General population:

Multiple studies were conducted among village residents in high HCV prevalence areas .The overall prevalence in rural areas averaged about 20%, higher than the national average. A study conducted in Kalama, a village in the Nile Delta, reported HCV prevalence of 40% among village residents ***(Darwish MA et al., 2001)***.

(Fig.2).

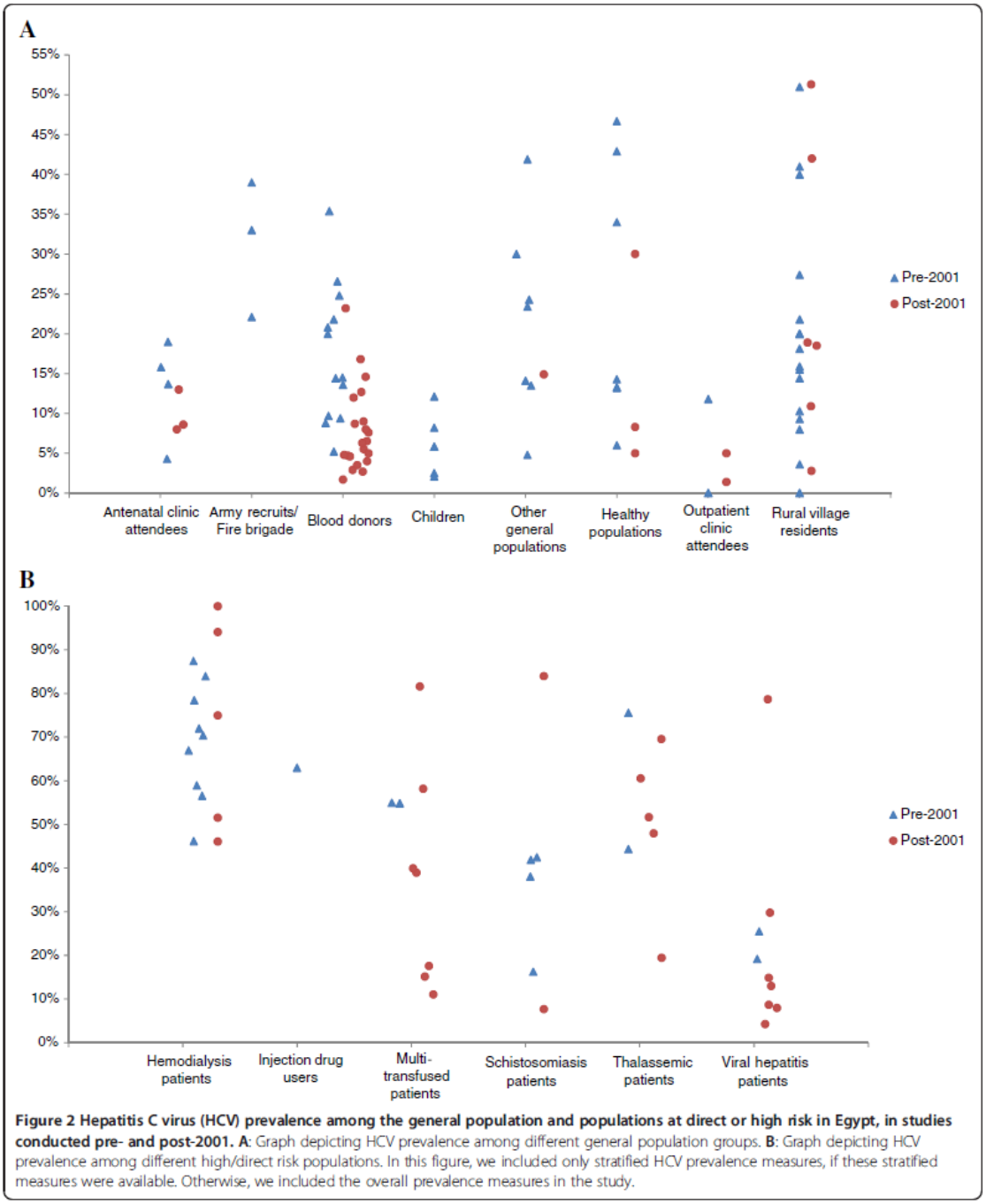

Figure 2 Hepatitis C virus (HCV) prevalence among the general population and populations at direct or high risk in Egypt, in studies conducted pre- and post-2001. A: Graph depicting HCV prevalence among different general population groups. **B**: Graph depicting HCV prevalence among different high/direct risk populations. In this figure, we included only stratified HCV prevalence measures, if these stratified measures were available. Otherwise, we included the overall prevalence measures in the study.

Figure 2 depicts the range of prevalence within each subgroup in studies conducted pre- and post-2001.

Among blood donors, studies appear to cluster at lower HCV prevalence levels post- 2001 infection control programs, compared to pre-2001. However, no distinct pattern can be observed within each of the other subgroups. (Mohamoud et al. BMC Infectious Diseases 2013).

Globally, the major risk factors for HCV infection are blood transfusions from unscreened donors and intravenous drug use. However, exposure to HCV-infected blood from other health-care-related procedures and regional cultural practices are increasingly recognized as having an important function in HCV transmission in some parts of the world. Since the introduction and improvement in the 1990s of the screening of blood donors, HCV transmission by blood transfusions is now exceedingly rare (around or less than one per million) in developed countries ***(Dodd RY et al., 2002).***

Unfortunately, the screening of blood donors for HCV is not yet routinely performed by some blood banks in developing countries ***(Prati D et al., 2006)***.

Most new cases in developed countries are related to intravenous drug use. Health-care-related procedures leading to nosocomial HCV transmission are not restricted to hemodialysis facilities. Several reports from Western countries have clearly documented nosocomial transmission of HCV through inadvertent sharing of multidose vials or unsterilized instruments, among others ***(Lesourd F et al., 2000).***

Similar nosocomial transmission of HCV outside dialysis units is certainly not less likely to occur in developing countries but has not been reported until now. Additional risk factors for HCV transmission include occupational exposure, especially by accidental needlestick, as well as perinatal transmission (about 6%), whereas the transmission of HCV by sexual activity appears relatively inefficient ***(Terrault NA ,2002).***

In Egypt, the major route of exposure appears to be due to injection therapy and inadequate infection control practices. In addition to blood transfusions prior to 1994, the major risk factor associated with HCV