Prevalence of HCV and HBV in Incident Hemodialysis Patients

THESIS

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Abstract

Background: HCV is major problem in hemodialysis unites. Prevalence of HCV increases nearly 87.5% among patients kept on regular hemodialysis for than 6 months .This high prevalence is not known either it is from dialysis or from increase risk of infection among patients having CKD. In Egypt less than 5% of hemodialysis has HBV detected by serological markers.

Objectives: Was to study HCV AB and HBsAg serology among incident hemodialysis patients admitted to hemodialysis units for the first time.

Methods: In this study, we studied 1000 patients adult ESRD patients recently admitted to dialysis unites in Cairo, each was subjected to the following serological tests:

HBsAg., HCV Ab.and HIV Ab

The prevalence of these different viruses was estimated among this group of patients.

Results:

- In our study the prevalence of HCV was 22.9%.and the prevalence of HBV was 1.4%.and the combined HCV and HBV infections were only 0.4%.
- The commenst age group of starting hemodialysis was between 51 years old to 60 years old .And the mean age was 49.42 years. And there were no great difference between males and females.

In conclusion: the mean age of hemodialysis patients in our unit was 49 years , we have a lower prevalence of hepatitis B in comparison to other countries in the middle east area, on the contrary we have the higher prevalence of hepatitis C in the middle east area., HCV infection is endemic among dialysis centers in Egypt.

Keywords: **CKD, CRF, dialysis, HCV and HBV.**

Introduction

Hepatitis C virus (HCV) belongs to the *Flaviviridae* family of viruses. Its genome is a single-stranded RNA molecule (genomic HCV-RNA). Virus replication involves the synthesis of a complementary RNA (antigenomic HCV-RNA) that acts as a template for production of genomic HCV-RNA.

Despite screening of blood products for anti-HCV and implementation of precaution measures, HCV infection is still a major problem in hemodialysis (HD) units ***(Barril, et al., 2008).***

With the notable exception of parts from Eastern Europe, hepatitis C incidence and prevalence are low among the European countries. Epidemiology, dialysis practice and reimbursement are significantly different across the world ***(Covic et al., 2009).***

The overall prevalence infection of hepatitis C among adult Egyptian population ranges between 14.4% ***(Darwish et al., 1992)*** and 22.5% ***(Farghaly and Barakat et al., ١٩93).*** However, this prevalence tremendously increases to reach nearly 87.5% among patients kept on regular hemodialysis for more than 6 months. It is not known if this very high prevalence among the dialysis population is due to increased risk of infection during dialysis or possible increase of infection among patients having CKD ***(Sharaf El-Din, et al. ٢٠٠٣).***

In Egypt less than 5% of adult hemodialysis patients has HBV ***(Gohar et al., 1995),*** detection of serological markers is the mainstay of diagnosis of HBV infection and the most reliable marker of HBV carriage is HBV surface antigen (HBsAg) in serum ***(Krogsgaard et al., 1985).***

Aim of the Work

The aim of this epidemiological trial is to study the HCVAb and HIVAb serology and HBV antigenemia among incident CRF patients admitted to hemodialysis unit for the first time.

Patients and methods:

This study will include 1000 adult ESRD patients recently admitted to dialysis units in Cairo city, each patient will subjected to the following serological tests:

1- HBsAg

2- HCV Ab

3- HIV Ab

The prevalence of these different viruses will be estimated among this group of patients looking for any possible odds ratio of co-infection.

Hepatitis C Virus

The hepatitis C virus (HCV) is a small RNA virus belonging to the genus *Hepacivirus* and family Flaviridae ***(DiBisceglie et al., 2000).***

History and classification:

The agent of parenterally transmitted non-A, non-B hepatitis remained elusive. Its existence was recognized by transmission of hepatitis to recipients of blood that had been tested for HbsAg and thereafter by the experimental infection of chimpanzees ***(Alter, 1995).***

Filtration experiments showed that the size of the agent was between 50 and 80nm. Its low density and sensitivity to organic solvents suggested that it was enveloped ***(DiBisceglie et al. 2002).***

Structure of the virus particles:

The virus is an enveloped particle of moderate size, it is of RNA genome. The density of the infectious virus is determined at 1.105 g/ml but lower densities could not be excluded ***(Bradley, 1991).***

After the identification of HCV sequences, further efforts to characterize the virus used the PCR for the detection of HCV-RNA in order to determine the density, size and abundance of the virus particle. Since HCV cannot be grown efficiently in cell culture, plasma sample from HCV-infected individuals were analyzed.

A study by ***(Thomssen, 1993)*** revealed surprising heterogeneity and variability of the HCV-RNA associated particles. The buoyant density of the particles is between less than 1.02 and 1.25 g/ml in sucrose-gradient centrifugation and varies from patient to patient

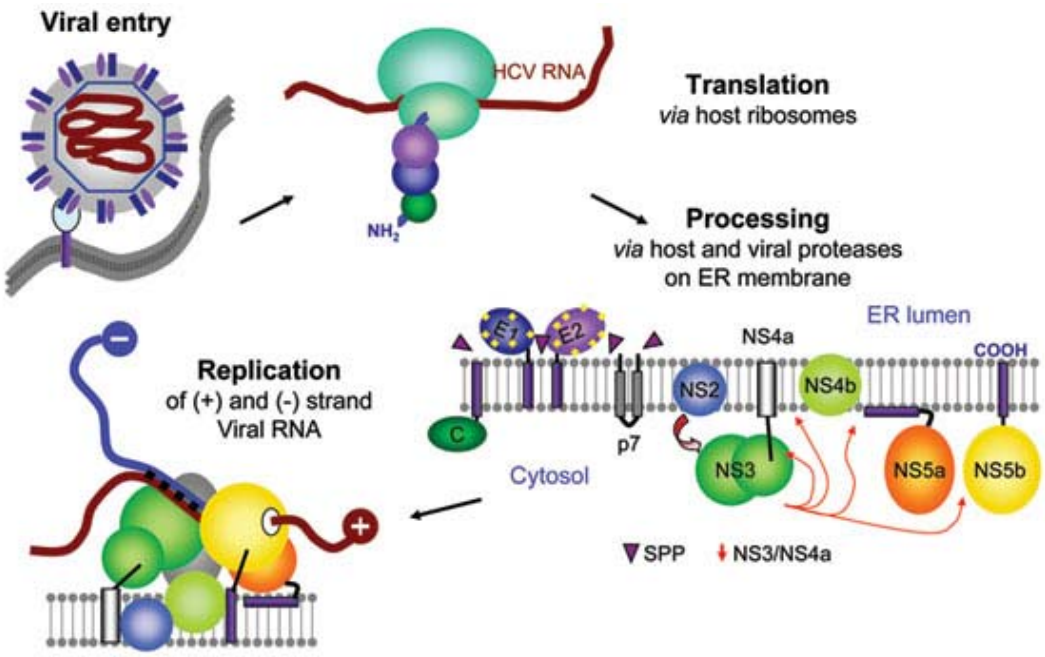

Fig (1): HCV life cycle (Thomssen, 1993)

Source of the infection and disease:

The source of the infectious material is usually blood, plasma, or Serum from infected individuals ***(Alter, 1995).***

A low infectivity, such as 10^2 infectious units/ml was correlated with a high number of HCV genome equivalents to 10^7 infectious units/ml ***(Hijikata. 1993).*** Usually the numbers of HCV particles and the infectivity in serum are high during the incubation phase, later the number of particles is highly variable but infectivity is usually lower ***(Oxford Hep, 1999).*** HCV is usual1y both free in the serum and bound to

leucocytes, but in some rare cases, leucocytes may contain HCV-RNA whereas the serum reacts negatively. Depending on the dose of the infectious agent and possibly, the viral quasispecies, HCV will rapidly (within a few weeks or even days) induce a viraemia detectable by a sensitive RNA-amplification technique, without recognizable symptoms ***(Oxford, 1999).***

In contrast to HAV and HBV, serum alanine transaminases rises significantly before HCV antibodies are detectable, usually 5-12 weeks after infection (extreme values at 2-26 weeks). Acute disease may result with resolution within several months. Increased viral diversity during the acute phase of hepatitis was found to be associated with progression to chronicity whereas resolving acute hepatitis was associated with relative stasis of the quasi species ***(Farci, 2000).*** Patients who respond to interferon therapy also have a decrease in viral genetic diversity and in the number of viral qasispecies **(Adrian *et al., 2002).***

In up to 85% of cases, viraemia persists in the presence of anti HCV about 45% of patients with acute hepatitis develop histologically confirmed chronic hepatitis ***(Oxford. 1999).***

Chronic hepatitis may proceed with variable activity; it usually takes decades until cirrhosis or hepatic failure becomes apparent ***(Thierry et al., 2001).***

Chronic hepatitis C varies in its course and outcome. At one end of the spectrum are patients who have no signs or symptoms of liver disease and completely normal levels of serum liver enzymes, liver biopsy usually shows some degree of chronic hepatitis. But the degree of injury is usually mild, and the overall prognosis may be good. At the other end of the spectrum are patients with severe hepatitis C who have symptoms, HCV-RNA in serum, elevated serum liver enzymes, who ultimately

develop cirrhosis and end-stage liver disease. In the middle of the spectrum are many patients who have few or no symptoms, mild to moderate elevation in liver enzymes, and an uncertain prognosis.

Researchers estimate that at least 20% of patients with chronic hepatitis C develop cirrhosis, a process that takes 10 to 20 years. After 20 to 40 years, a smaller percentage of patients with chronic disease develop liver cancer ***(NIDDK, 2002).***

Risk factors and transmission:

HCV is spread primarily by contact with blood and blood products. Blood transfusion and the use of shared, unsterilized, or poorly sterilized needle and syringes have been the main causes of spread of HCV ***(Laskus et al., 1990).***

The major high-risk groups for hepatitis C are:

- People who had transfusions before June 1992, when sensitive tests for anti-HCV were introduced for blood screening ***(Tremolada et al., 1991).***
- People who have frequent exposure to blood products.
- These include patients with hemophilia, solid-organ transplants, chronic renal failure, or cancer requiring chemotherapy ***(Laskus et al., 1990).***
- Health care workers who suffer needle-stick accidents ***(Kiyosowa el al., 1994).***
- Injection drug users, including those who used drugs briefly many years ago ***(Kiyosowa et al., 1994).***

- Infants born to HCV -infected mothers ***(Lam, 1993).***

Other groups who appear to be at slightly increased risk for hepatitis C are:

- People with high-risk sexual behavior, multiple partners and sexually transmitted diseases.
- People who use cocaine, particularly with intranasal administration, using shared equipment.

Extrahepatic manifestation of chronic HCV infection:

Complications that do not involve the liver develop in 1 to 2 percent of people with hepatitis C the most common is cryoglobulinemia, which is marked by:

- Skin rashes, such as purpura, vascular or urticaria ***(Hans et al., 1996).***
- Joint and muscle aches.
- Kidney disease.
- Neuropathy.
- Cryoglobulins, rheumatoid factor and low complement level in serum ***(Lunel et al., 1994).***

Other complications of chronic hepatitis C are:

- Glomerulonephritis ***(Harle et al., 1993).***
- Porphyria cutanea tarda.

Diseases that are less well documented to be related to hepatitis C (NIDDK 2002) are:

- Seronegative arthritis.
- Kerato-conjunctivitis sicca (Sjogren's syndrome).
- Non-Hodgkin's type, B-cell lymphomas.
- Fibromyalgia.
- Lichen plannus.

Approach to diagnosis:

A variety of tests are available for hepatitis C diagnosis. Test that detect anti HCV include the enzyme immunoassay (EIAs) which contain HCV antigens from the core and non structural genes, and recombinant immunoblot assay (RIBAs) which contain the same HCV antigens as ElA in an immunoblot format ***(Jay et al., 1997).*** The EIA tests are reproducible, inexpensive and have been automated. They are suitable for screening low-and high prevalence population and as initial tests for patients with clinical liver disease ***(Jay et al., 1997).*** The RIBA test is most frequently used as a supplementary assay.

HCV Infection Among Chronic Hemodialysis Patients

Hepatitis C virus (HCV) is a major public health problem and is the most common liver disease among hemodialysis (HD) patients. The seroprevalence of HCV infection among HD ranged from 1.9% to 80% in reports published since 1999.

The main risk factor for HCV acquisition in HD patients seems the length of time on HD. Phylogenetic analysis of HCV viral isolates has suggested nosocomial patient-to-patient transmission of HCV infection among HD patients. Lack of strict adherence to universal precautions by staff and sharing of articles such as multidose drugs might be the main mode of nosocomial HCV spread among HD patients ***(Yen et al., 2003).***

Hepatitis C virus (HCV), infecting about 170 million persons worldwide, is a major public health problem (Global surveillance and control of hepatitis C, 1999). An estimated 5-20% of HCV infected patients has or will develop cirrhosis, 1-4% of whom will annually develop hepatocellular carcinoma. Well-known risk factors for HCV transmission include injection drug use, blood product transfusion, organ transplantation, chronic hemodialysis (HD), occupational exposure among health care workers, unprotected sexual contact, and vertical transmission ***(Strader et al., 2004).***

The relation between HCV infection and kidney disorders is well recognized. Hepatitis C infection has been associated with essential mixed cryoglobulinemia that may lead to membranoproliferative glomerulonephritis ***(Johnson et al., 1993).***

On the other hand, patients with renal disease have been at increased risk of acquiring HCV because of prolonged vascular access as well as the potential for exposure to infected patients and contaminated equipment. Liver disease is a significant cause of morbidity and mortality in patients with end-stage renal disease (ESRD) treated by dialysis or transplantation and hepatitis C is the most common liver disease in renal dialysis patients ***(Fabrizi et al., 2002).***

HCV Global Epidemiologic Features in HD Population

The prevalence of HCV infection varies greatly among various populations of patients on HD from different geographic regions. In a review of so far published data in 1999, ***(Wreghitt et al., 1999)*** described HCV prevalence among HD population ranging from 4% in the UK to 71% in Kuwait. Some investigators suggested a decline in HCV prevalence among HD patients in recent years, mostly attributable to strict adherence to universal precautions and with or without observing isolation measures ***(Jadoul et al., 2004).***

The reported anti-HCV positivity since 1999 ranged from 1.9% in the Slovenian 2001 annual report ***(Buturovic-Ponikvar et al., 2003)*** to 80% in Senegal ***(Diouf et al., 2000).*** The HCV seroprevalence in HD population was 59% in Bosnia and Herzegovina ***(Ahmetagic et al., 2006),*** 6.8% in Belgium ***(Jadoul et al., 2004),*** 16.3% in France ***(Salama et al., 2000),*** 6.1% in Germany ***(Hinrichsen H et al., 2002),*** 10 – 29% in Greece ***(Rigopoulou et al., 2005),*** 22.5-32.1% in Italy ***(Petrosillo et al., 2001),*** 75% in Moldavia ***(Covic et al., 1999),*** 3.4% in the Netherlands ***(Schneeberger et al., 2000),*** 11% in Sweden ***(Almroth et al., 2002),*** 7-23.3% in the USA ***(Kalantar-Zadeh et al., 2007),*** 20.5% in Libya ***(Daw et al., 2002),*** 23.7% in Sudan ***(El-Amin et al., 2007),*** 19-41.7% in Tunisia ***(Bouzgarrou et al., 2005),*** 8.4-43.2% in Brazil ***(Albuquerque et al., 2005),*** 6.7% in Mexico ***(Mendez-Sanchez et al., 2004),*** 59.3% in Peru ***(Sanchez et al., 2000),*** and 3.5% in Puerto Rico ***(Lopez-Navedo et al., 1999),*** 70.7% in Egypt ***(Alaa Sabry et al. 2007).***

The studies that prospectively followed HD patients for their HCV status presented an annual incidence rate of de novo HCV infection of 0.4% in France ***(Izopet J et al., 2005),*** 0.5% in Tunisia ***(Izopet J et al., 2005),*** 0.5% in the Netherlands ***(Schneeberger et al., 2000),*** 0.83% in

Italy ***(Lombardi M et al., 1999),*** 1.38% ***(Fabrizi et al., 2005)*** and 2.1% ***(Fabrizi et al., 1999)*** in the USA, 0.33% ***(Kumagai et al., 2005),*** 2.59% ***(Furusyo et al., 2001),*** and 3.1% in Japan ***(Fissell et al., 2004),*** 3.7% ***(Moreira et al., 2003)*** and 5.5% in Brazil ***(Santos et al., 2007),*** and 6.2% in Greece ***(Sypsa et al., 2005).***

Almost all recent surveys on the subject have congruently suggested the length of time on HD as a risk factor for HCV seropositivity ***(Kalantar-Zadeh et al., 2007).*** Historically, the number of blood transfusions received was consistently reported in the literature to be associated with increased prevalence of HCV positive dialysis patients ***(Wreghitt et al., 1999).*** However, several recent reports could not recognize blood transfusion as an independent risk factor in HCV spread among HD subjects ***(El-Amin et al., 2007).*** Indeed, erythropoietin prescription from the late 1980s onward reduced the HD patients' need to blood transfusion.

Furthermore, introduction of sensitive tests for the screening of blood donors has markedly reduced the risk of HCV transmission through blood product transfusion. These two main reasons may explain recent findings on the lack of association between blood transfusion and HCV infection. History of organ transplantation ***(Sypsa et al., 2005),*** older age ***(Fabrizi et al., 2005),*** younger age ***(Kalantar-Zadeh et al., 2007),*** dialysis in multiple centers ***(Hosseini-Moghaddam et al., 2006),*** the HD unit ***(Santos et al., 2007),*** hepatitis B infection ***(Fissell et al., 2004),*** human immunodeficiency virus infection ***(Fabrizi et al., 2005),*** and diabetes mellitus ***(Ocak et al., 2006)*** were other factors that were suggested by some studies to be associated with HCV positivity.

Diagnostic Features