Molecular epidemiology and clinical importance of TT virus infection in Haemodialysis Patients, South of Iran

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Abstract: Patients on hemodialysis are considered to be at risk of infection by blood-borne viruses and a prevalence of Transfusion transmitted infection has been reported in patients on hemodialysis in many countries. According to the lack of data about the prevalence of TTV in Jahrom (a city in south-west of Iran), this study was conduted to investigate the molecular prevalence of TTV viremia among hemodialysis patients in this south-west city of Iran. In this cross sectional study serum samples from HCV and HBV negative 711 patients on maintenance hemodialysis for molecular prevalence of TT virus in south of IRAN, April, 2013. Serum samples taken before dialysis from each subjects were tested for molecular and biochemical analysis. Some possible risk factors of TT virus infection including: age, gender, duration of hemodialysis treatment and serum aminotransferases (AST and ALT) levels were collected from each studied population. Data were analyzed by use of parametric and non-parametric analyses with SPSS for Windows. TTV infection was detected in 27.80% of the patients. In haemodialysis patients, no association was found between TTV infection and the demographic parameters (age, sex), but we found statistically significant difference were present between these groups for what concern time on haemodialysis therapy, ALT and AST levels. The prevalence of TTV infection among hemodialysis patients reported by other authors is similar to our or even higher. According to the finding of present study TTV is presented as one of probable agent of hepatitis in haemodialysis patients.
[Jahromi AS, Erfanian S, Farjam MR, Madani A. **Molecular epidemiology and clinical importance of TT virus infection in Haemodialysis Patients, South of Iran.** *Life Sci J* 2014;11(2):182-185]. (ISSN:1097-8135). http://www.lifesciencesite.com. 26

Keywords: TT Virus; Haemodialysis patient; Epodemiology; ALT; AST

1. Introduction

Patients with chronic renal failure on maintenanceare are at high risk of acquiring parenteral infections. Of these, hepatitis B (HBV) (Fabrizi et al. 2002) and hepatitis C (HCV) (Fabrizi et al. 1997) infections have been the most important infections transmitted among dialysis patients. More recently, most episodes of hepatitis acquired in patients on maintenance hemodialysis were other than A to E hepatitis, and some studies have shown that hepatitis G virus (HGV) might account for some of these infections (Huang et al. 2001, Pourahmad et al. 2009).

However, the etiology of a substantial proportion of hepatitis in uremic patients remained undefined, suggesting the existence of additional causative agents.

Torque teno virus is a human non-enveloped single-stranded circular DNA virus with icosahedral symmetry and a particle size of approximately 30 nm. TTV was first characterized as a blood-borne virus and was initially referred to as transfusion-transmitted virus (Nishizawa et al. 1997).

Transfusion transmitted (TT) virus originated through a search focused on viral causes of undefined post-transfusion hepatitis, idiopathic chronic liver disease and fulminant hepatic failure (Okamoto et al. 1998, Shoeib et al. 2011).

Torque teno virus is a human non-enveloped single-stranded circular DNA virus with icosahedral symmetry and a particle size of approximately 30 nm. TTV was first characterized as a blood-borne virus and was initially referred to as transfusion-transmitted virus. TT virus previously classified under the Circovirus genus, get its new name: TorqueTenoVirus and placed under the Anellovirus genus belong to the Circoviridae family (Nishizawa et al. 1997). TT virus DNA detectable in liver tissues of infected patients in high titres than serum suggesting that TT virus is hepatotropic and can be found in a proportion of patients with different non-A-G hepatitis (Okamoto et

al. 1998, Lopez-Alcorocho et al. 2000). The majority of TT virus infected patients had no biochemical or histological evidence of significant liver damage (Erensoy et al. 2002).

Patients on hemodialysis are considered to be at risk of infection by blood-borne viruses (Tarrass et al. 2006) and a prevalence of TTV infection has been reported in patients on hemodialysis in many countries (Massaú et al. 2012 Irshadet al. 2010, Rivanera et al. 2009, Kristian et al. 2006, Touinssi et al. 2001, Chattopadhyay et al. 2005, Hsu et al. 2007, Kheradpezhouh et al. 2007).

According to the lack of data about the prevalence of TTV in Jahrom (a city in south-west of Iran), this study was conduted to investigate the molecular prevalence of TTV viremia among hemodialysis patients in this south-west city of Iran.

2. Material and Methods

In this cross sectional study serum samples from HCV and HBV negative 711 patients on maintenance hemodialysis including 406 (57.10%) males and 305 (42.90%) females, 20.0- 88.0 years old (58.62±15.26 year) were investigated for molecular prevalence of TT virus in south of Iran, April, 2013.

This study was approved by ethics committee in medical research in Jahrom University of medical sciences.

Serum samples taken before dialysis from each subject were stored at -70°C until use for molecular and biochemical analysis.

Some possible risk factors of TT virus infection including: age, gender, duration of hemodialysis treatment and serum aminotransferases (AST and ALT) levels were collected from each studied population.

The serum levels of ALT and AST were determined in the patients by related analyzing kits (Pars Azmoon-Iran) according to the manufacturer's directions.

The DNA genome of TT virus was extracted from all serum samples the patients by DNPTM Kit (CinnaGen-Iran) according to manufacturer's directions.

The molecular detection of TT virus-DNA genome was investigated by an in-house semi nested-PCR as protocoled in our previous study (Azinfar et al. 2012).

The significant relationships of molecular prevalence of TT virus infection in hemodialysis patients with probable studied risk factors were analyzed by use of parametric and non-parametric analyses with SPSS for Windows (version 15, Chicago, IL, USA) and P-value of less than 0.05 was considered significant.

3. Results

In present study TTV infection was detected in 27.80% of the patients (198/711) also 19.80% of our patients (141/711) had the history of transfusion.

Mean serum levels Alt and AST of enrolled subjects were 39.24±48.99 unit/lit and 46.90±53.68 unit/lit respectively. Mean time on hemodialysis therapy in the patients was 24.29±13.99 mounts and number of hemodialysis per week 2.49±0.65.

It was found a high prevalence of history of transfusion among TTV- DNA positive patients (120/198; 60.60%) when compared with TTV- DNA negative patients (21/513; 4.1%; $P<0.001$; $\chi 2$ test).

In haemodialysis patients, no association was found between TTV infection and the demographic parameters (age, sex), but we found statistically significant difference were present between these groups for what concern number of hemodialysis per week, time on haemodialysis therapy, mean serum levels of ALT and AST (Table 1).

Table 1. Characteristics of TTV- DNA positive and TTV- DNA negative patients

TTV- DNA	Positive	Negative	P value
Number of patients	198/711 (27.80%)	513/711 (72.20%)	---
Sex (M/F)	82/116	223/290	0.673
Age (mean±SD)	57.88±15.47 (range 20–81)	58.91±15.18 (range 20–88)	0.783
Time on haemodialysis therapy (mean±SD) months	28.12±14.275 (range 3–78)	22.81±13.608 (range 2–68)	0.001
number of hemodialysis/ week (mean±SD)	2.64±0.52	2.43±0.68	0.001
History of transfusion	120/198; (60.60%)	21/513(4.1%)	0.001
AST unit/lit (mean±SD)	109.91±68.45	22.58±8.06	0.001
ALT unit/lit (mean±SD)	102.65±54.20	14.77±6.59	0.001

4. Discussions

This study describes the prevalence and association of Torque teno virus (TTV) infection in patients with chronic renal failure (CRF) on maintenance hemodialysis (HD). TTV infection was diagnosed by detection of TTV-DNA in serum, using the polymerase chain reaction (PCR) technique. TTV-DNA was estimated in a total number of one hundred patients with CRF.

The prevalence (27.80%) detected among these patients was in the range of TTV prevalence observed among patients undergoing haemodialysis from other countries, which ranged from 16-58.5% (Martinez et al. 2000, Irshad et al. 2010, Afkari et al. 2012) but it was lower than TTV prevalence (68.8%) in Brazilian haemodialysis patient (Massaú et al. 2012).

This study demonstrate association between TTV infection and history of transfusion which consistent with other researches (Afkari et al. 2012, Massaú et al. 2012) but not with the finding of a study in Taiwan (Hsu et al. 2007).

Interestingly, present study demonstrate a significant association between TTV infection and the duration of haemodialysis treatment, serum level of AST and ALT. These findings are not in agreement with the results of other previous studies (Hsu et al. 2007, Kheradpezhouh et al. 2007, Martinez et al. 2000).

Such differences may be explained by the existence of different routes of virus transmission and lifestyle differences among different populations around the world. Also the present study was done on HCV and HBV negative haemodialysis patients.

The prevalence of TTV infection in south of Iran matches that of observations in Iran and other countries. The prevalence of TTV infection among hemodialysis patients reported by other authors is similar to our or even higher.

According to the finding of present study TTV is presented as one of probable agent of hepatitis in haemodialysis patients.

The pathology of TTV and the host response to TTV infection warrant further investigation.

Acknowledgements:

Authors are grateful to the Student Research Committee of Jahrom University of Medical Sciences for financial support to carry out this work. This article has been extracted for Ms Mahsa Moghaddam Thesis for her general physician degree.

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1/15/2014