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Seroprevalence of hepatitis B virus and hepatitis C virus; its incidence and risk factors in incident chronic kidney disease (CKD) stage – V patients on hemodialysis in a tertiary care centre

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Abstract

Introduction: End stage renal disease (ESRD) has become a universal public health problem. Chronic kidney disease (CKD) is immune deficient state. So, they may be infected with hepatitis B virus (HBV) and hepatitis C virus (HCV) during hemodialysis. This becomes an important cause of morbidity and mortality among patients of hemodialysis.

Objectives: To find out the seroprevalence and incidence rate of hepatitis B and hepatitis C infections in CKD patients on hemodialysis in a tertiary care hospital.

Material and methods: A total of 380 blood samples were collected from CKD stage V patients on hemodialysis. The serum samples tested for HBsAg and anti-HCV by Vitros ECiQ (Ortho Clinical Diagnostics) system, 3rd generation. Positive results for HBsAg & anti-HCV reactive by chemiluminescence method (VITROS ECiQ), was confirmed by enzyme-linked fluorescent immunoassay method by using mini VIDAS, BioMerieux. Results: Seroprevalence of hepatitis C virus (6.57%) is higher than hepatitis B virus (1.84%). Incidence rate of HBV is 5.2 per 1000 cases in the institution. The incidence rate of HCV is 0 per 1000 cases per year.

Discussion: In the present study, the prevalence of HBV infection in HD patients was 1.84% and the prevalence of HCV infection in HD patients was 6.57%. The variations in prevalence of HBV and HCV depend mainly on the strict adherence to universal infection control precautions. This will decrease the HBV and HCV prevalence rate among these patients. Conclusion: Chronic renal failure (CRF) patients who undergo repeated HD are at high risk of developing HBV and HCV. Proper monitoring for the early detection is required. Blood-transfusion, duration of dialysis, vaccinations are important risk factor for infection.

Keywords: seroprevalence; hepatitis B virus; hepatitis C virus; chronic kidney disease; hemodialysis

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Introduction

End stage renal disease (ESRD) has become a universal public health problem worldwide [1-2], due to increased prevalence of diabetes mellitus [3] and hypertension [4]. In western countries, diabetes and hypertension account for over 2/3rd of the cases of chronic kidney disease (CKD) [5]. In India, diabetes and hypertension today account for 40–60% cases of CKD [6]. Among these subjects, 25–40% is likely to develop CKD and hence, the ESRD burden will rise. Conventional hemodialysis remains the most common treatment for ESRD worldwide, and is usually performed for 3–5 h, three days per week [7, 8].

CKD is defined as any abnormality of kidney structure or function, present for > 3months, with implications of health. The stages of CKD according to Kidney Disease: Improving Global Outcomes (KDIGO) guideline is described in Table 1.

Table 1: CKD classification and staging according to KDIGO guidelines.

CKD Classification and Staging Green: Low risk (LR) Yellow: Moderate risk (MR) Orange: High risk (HR) Red: Very high risk (VHR)				Kidney damage stage Urine albumin/creatinine ratio Description and range		
				A1	A2	A3
				Normal to mild increase <30mg/g	Moderate increase 30-300 mg/g	Severe increase >300mg/g
Kidney function stage GFR (ml/min/1.73m²) Description and range	G1	Normal or high	≥90	LR	MR	HR
	G2	Mild decrease	60-89	LR	MR	HR
	G3a	Mild to moderate decrease	45-59	MR	HR	VHR
	G3b	Moderate to severe decrease	30-44	HR	VHR	VHR
	G4	Severe decrease	15-29	VHR	VHR	VHR
	G5	Kidney failure	<15	VHR	VHR	VHR

CKD is immune deficient state; hence, they may be infected with hepatitis B virus (HBV) and hepatitis C virus (HCV) during hemodialysis. Eventually, HBV and HCV infection is an important cause of morbidity and mortality among patients of hemodialysis [9].

Hepatitis C virus is more common in dialysis patients than in healthy populations and decreased survival among patients with chronic kidney disease stage V patients [10, 11]. There is large variability in prevalence among countries and within countries, among hemodialysis centers [12]. Risk factor for hepatitis B and C in dialysis patient includes the number of blood products received [13], dialysis vintage [14], the prevalence of hepatitis B and hepatitis C infection within individual dialysis unit [14] and male gender [15, 16].

In the present study, screening done to know the seroprevalence of HBV and HCV infection in all CKD stage V patients under dialysis were screened for HBV and HCV infections from September 2015 to August 2016 (one year). Since CKD stage V patients have impaired immune system, the study was emphasized to know the seroprevalence of HBV and HCV infection and to assess their risk of transmission, to calculate mean age and to find gender predominance.

To find out the seroprevalence and Incidence rate of hepatitis B and hepatitis C infections in CKD patients on hemodialysis in a tertiary care hospital. The objectives are (1) To screen HBV and HCV infection in CKD stage V patients on hemodialysis; (2) To assess the risk factors of HBV and HCV infection: role of blood transfusion, vaccination and dialysis vintage; (3) To calculate mean age and to find gender predominance.

Material and methods

The present study was conducted in the Department of Microbiology, and Dialysis unit of Nephrology, Krishna Institute of Medical Sciences, Secunderabad, India from September 2015 to August 2016 (one year). It is a prospective, observational and longitudinal study. A total of 380 blood samples were collected from CKD stage V patients on hemodialysis attending outpatient Department of Dialysis unit, Krishna Institute of Medical Sciences, Secunderabad, India. The serum samples were tested for HBsAg and anti-HCV by Vitros ECiQ (Ortho Clinical Diagnostics) system, 3rd generation. Principles of the procedure or HBsAg detection & anti-HCV detection in VITROS ECiQ (Ortho Clinical Diagnostics) is based on chemiluminescence method [17].

Inclusion criteria: All old and new cases of seronegative and seropositive (HBV and HCV) patients undergoing dialysis; patient who are transferred from other dialysis units; patients undergoing blood/blood products transfusion; patient receiving and not receiving vaccination; patient undergoing transplantation; age group: >18yrs-80yrs.

Exclusion criteria: Hepatitis A, E, D virus infected patients are not included; age group < 18 years to > 80years; pregnant women.

Statistical analysis

After taking ethical committee permission, patients were enrolled in study. Eligible patients were included into study after obtaining written informed consent. The study population was divided into groups based on incidence of hepatitis B and/or HCV or no infection. The differences between the groups for continuous variables were analyzed using independent student t-test. A $p < 0.05$ was considered statistically significant. After data collection and preparation of master sheet, analysis was done by using Statistical Package for Social Sciences (SPSS) version 20.0 for Windows, IBM Computers, New York, USA.

The blood samples were collected in yellow gel vacutainer by venepuncture following the standard precautions. The collected blood samples were transported to the Department of Microbiology. It was then centrifuged at 3500 rpm for 20 min and the serum gets separated. Serum samples were refrigerated (2-8°C) or stored frozen in a deep freezer (-20°C), if not tested within two days.

All 380 serum samples were tested for the seroprevalence of HBV and HCV infection by determining the presence of HBsAg and anti-HCV antibodies using a 3rd generation VITROS ECiQ (Ortho Clinical Diagnostics). Screening parameters were HBsAg and anti-HCV by Vitros ECiQ (Ortho Clinical Diagnostics) system, 3rd generation. According to Institutional policy, a repeat testing was done every three months.

When a sample is found to be positive for HBsAg & anti-HCV reactive by chemiluminescence method (VITROS ECiQ), the test result is confirmed by testing enzyme-linked fluorescent immunoassay (ELFA) method by using mini VIDAS, BioMerieux.

Results

A total of 380 cases were included in the study, maximum number of cases were in the age group between 41 and 60 years (49.5%) and least number of cases were in the age group up to 20 years (1.8%) (Table 2).

Table 2: Age wise distribution.

Seroprevalence	*18-20 years*	*21-40 years*	*41-60 years*	*61-80 years*
Total	07 (1.8%)	59 (15.5%)	188 (49.5%)	126 (33.2%)
HBV	--	01 (14.3%)	05 (71.4%)	01 (14.3%)
HCV	--	05 (20%)	14 (56%)	06 (24%)
Co infection	--	--	01 (100%)	--

The Figure 1 shows mean age of HBV infection under hemodialysis is 50.14yrs and for HCV is 51.88years. The calculated p value is 0.9 by ANOVA ($p > 0.05$) and hence statistically not significant.

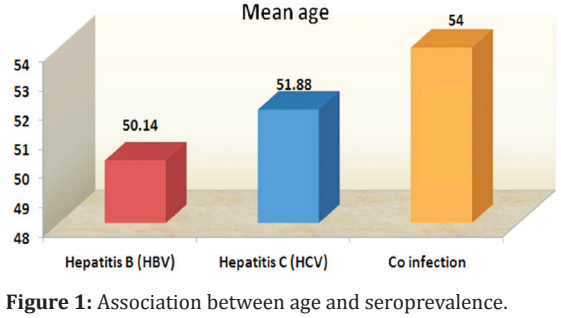

Figure 1: Association between age and seroprevalence.

The Figure 2 shows that males (n = 256; 67.36%) are more than females (n = 124; 32.63%). And also males are more prone to get infected by HBV and HCV infections. The calculated p value is 0.3 by Yates corrected chi square test ($p > 0.05$) and hence statistically not significant.

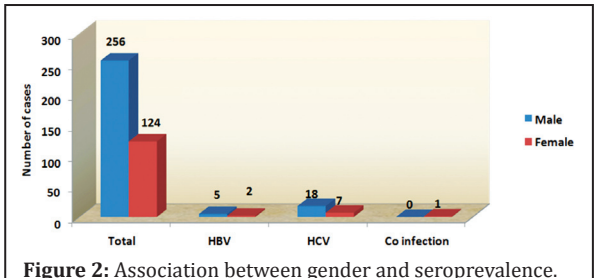

Figure 2: Association between gender and seroprevalence.

A total of 380 cases were included in the study, among them 137 were the old cases (including 5 HBV and 25 HCV positive cases) and 243 were the new cases (including 2 HBV positive cases) as shown in Table 3. Seroprevalence of hepatitis C virus (6.57%) is higher than hepatitis B virus (1.84%) (Table 4).

Table 3: Types of cases showing serological variation.

Types of case	*Seronegative patients (n = 348)*	*Seropositive patients (n = 32)*		*Total (n = 380)*
		HBV(n = 7)	*HCV(n = 25)*	
Old cases (n = 137)	107	5	25	137
New cases (n = 243)	241	2	0	243

Table 4: Seroprevalence of hepatitis B virus (HBV) and hepatitis C virus (HCV) in chronic kidney disease patients on hemodialysis.

Seroprevalence	*Number (n)*	*Percentage (%)*
Hepatitis B (HBV)	07	1.84%
Hepatitis C (HCV)	25	6.57%
Co infection	01	0.26%

The incidence rate of HBV is 5.2 per 1000 cases in the institution. The incidence rate of HCV is 0 per 1000 cases per year described in Figure 3.

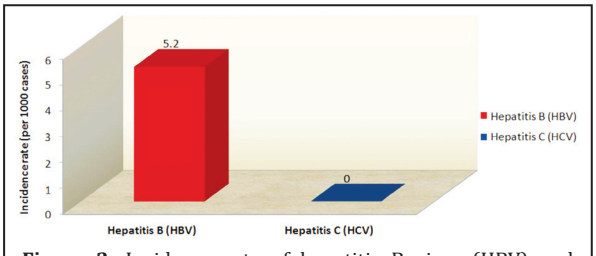

Figure 3: Incidence rate of hepatitis B virus (HBV) and hepatitis C virus (HCV) in chronic kidney disease patients on Hemodialysis.

The Figure 4 shows significant association between history of blood transfusion and HBV and HCV infections. Among all HCV positive patients, 36% patients had past history of blood transfusion. All HBV positive patients i.e. 100% of HBV infected patients, had history of previous blood transfusion. The p value is < 0.006 by Yates corrected chi square test (p < 0.05 hence statistically significant).

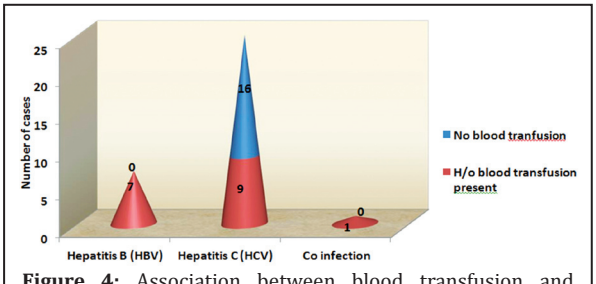

Figure 4: Association between blood transfusion and seroprevalence.

The Figure 5 shows the significant association between history of vaccination against HBV and HBV & HCV infections. The p value is < 0.04 by Yates corrected chi square test (p < 0.05 hence statistically significant). HCV infections are seen more in case of no history of vaccination against HBV.

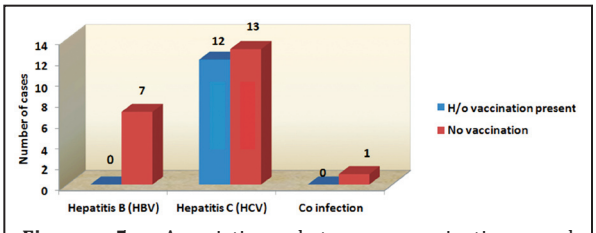

Figure 5: Association between vaccination and seroprevalence.

HCV infections are seen more in case of dialysis vintage ≥ 5years. HBV infections are seen in patients having dialysis vintage < 5years (Figure 6). The p value is < 0.02 by Yates corrected chi square test (p < 0.05 hence statistically significant).

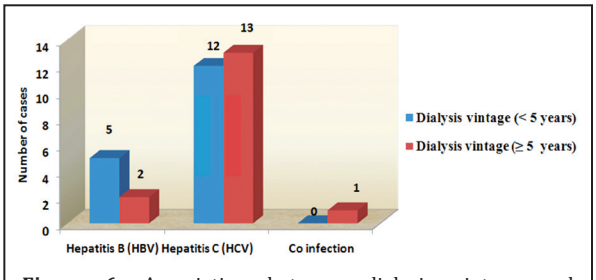

Figure 6: Association between dialysis vintage and seroprevalence.

Discussion

In the present study, the prevalence of HBV infection in HD patients was 1.84% and the prevalence of

HCV infection in HD patients was 6.57%. However, the prevalence of HBV among dialysis patients in India is reported to range between 3.4–43% [18, 19]. The prevalence of HCV infection in the western countries ranges between 4 and 23.3% [20, 21]. In contrast, a study done in Asian countries found the prevalence of HBV infection to be between 1.3% and 14.6% which is similar to this study [22]. A study by Burdick et al., showed a HBV prevalence of 0–6.6% across dialysis facilities in Western Europe, Japan, and the USA [23]. HCV prevalence in HD patients varies geographically both within and between countries. Some studies have suggested a decline in HCV prevalence among HD patients in the recent years, mostly due to universal precautions. Studies by Reddy et al., and Harmankaya et al., showed the prevalence of 4.7% and 5.9%, respectively [24].

The variations in prevalence of HBV and HCV depend mainly on the strict adherence to universal infection control precautions. Adherence to strict infection control and isolation measures also will decrease the HBV and HCV prevalence rate among these patients. In the present study, HCV (6.31%) prevalence was higher than HBV (1.84%) in HD patients, which correlates with an earlier study which reported the prevalence of HCV and HBV to be 20.2% and 13.3%, respectively, in HD patients [25]. Also the seroprevalence of HCV in CKD stage V patients on hemodialysis were comparatively higher (6.57%) than seroprevalence of HCV in general population of India (3.7%).

The present study showed that history of blood transfusion is significant (p value = 0.006) in transmission of HCV infection shown in Figure 2. Prior to effective screening of blood donations, HCV infection was associated with blood transfusions needed to correct the anemia associated with kidney disease [26, 27]. Patient to patient transmission in HD units is also reported [28, 29].

The blood transfusion data of HD patients showed that HBV and HCV infected patients had received blood transfusions compared (12.5% and 50% of HBV and HCV infected patients respectively) to the uninfected patients which was contradictory to report of Natov et al., which showed more number of transfusions in HCV infected patients [30]. However, another Indian study by Salunkhe et al. had not shown any difference in this context, and hence, it is difficult to establish a correlation between the number of transfusions and the HBV/HCV infections [31]. Several studies have shown that the risk of acquiring the HCV infection increase with an increase in the number of units of blood which were transfused [32].

Vaccination offers significant protection against HBV infection. Although, vaccine response rates are low and unpredictable in dialysis patients. Because of the impaired immune response, HD patients are given larger doses of the vaccine and sometimes revaccination to produce adequate antibody titer [33]. In the present study, vaccination against HBV showed a significant association (p value = 0.04) for protection against HBV infection. Among unvaccinated patients, the prevalence of HBV is 7% and HCV is 13% (Figure 3). In the absence of a vaccine, routine screening for infection and strict adherence to standard infection control practices are vital for preventing HCV transmission in HD units [34, 35].

In the present study, dialysis vintage of > 5years showed p value = 0.02, hence statistically significant (Figure 4). In concordance with the results, the Dialysis Outcome and Practice Pattern Study (DOPPS) showed that high HCV seroconversion was associated with a longer time on dialysis, and concluded that seroconversion was associated with an increase in the facility HCV prevalence, but not with the isolation of HCV-infected patients [36].

Various observations support the theory of transmission of HCV among HD patients including increasing duration of HD, the higher incidence of HCV in units with a high prevalence of infection, and the relative homogeneity of HCV isolates in patients receiving treatment in the same HD unit [37].

Conclusion

Chronic renal failure patients who undergo repeated HD are at high risk of developing HBV and HCV. They need to be monitored for the early detection of these infections. Blood transfusions played an important role in transmission of HBV and HCV in hemodialysis patients. Duration of dialysis plays an important risk factor for infection. As longer the dialysis vintage

there is more possibility of getting infected by HBV and HCV. To decrease the transmission of infection, the patients need to be segregated from the infected patients in the hospital and separate dialysis units have to be used for these infected patients. Prevention of uninfected patients with hepatitis B vaccination and treatment for HCV infected persons will decrease morbidity.

Acknowledgment

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Conflicts of interest

Authors declare no conflicts of interest.

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