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CASE STUDY

Study of prevalence of Hepatitis B and Hepatitis C and HCV genotypes in hemodialysis patients

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ABSTRACT

Background: Hepatitis B (HBV) and Hepatitis C virus (HCV) infections are the commonest cause of viral Hepatitis among Hemodialysis (HD) patients. Present study was carried out to find out of the prevalence of viral markers like HBsAg and Anti HCV in the newly diagnosed Chronic Renal Failure patients, taken for maintenance Hemodialysis. **Material and Methods:** Present study was hospital based, prospective cross sectional and multicentered study, conducted in patients of All age groups, both Genders, cases of Adult CKD taken for maintenance Haemodialysis, who had not received HBV vaccination at any point earlier, free from overt infection, immunosuppression & free from any chronic disease including autoimmune disorders. **Results:** Among 1705 patients, there were 1189 males (69.7%) and 516 were females.(30.3%) and their mean age was 42.6 years.At the initiation of hemodialysis, among the study population two of them were reactive to HbsAg, 15 to anti HCV and five were found to be having co-infection. The prevalence of HbsAg and Anti HCV and both among the study was 0.11%, 0.87% and 0.29% respectively.The distribution of HbsAg and Anti HCV among the healthy voluntary blood donors was 1.33% and 0.9% respectively. None of them carried both HbsAg and Anti HCV during the study period.Distribution of 22 males and 12 females on MHD carried one or other viral markers or both viral markers. HCV genotyping assay determined the Genotypes 1, 2,3,4,5 & 6 for the Anti HCV positive case, revealed that it belonged to genotype 3b. **Conclusion:** Seroconversion at the end of 3 months of MHD among the cases who were negative for HbsAg and Anti HCV was 0.25 and 0.5% respectively. Genotype 3b was identified in 16 (57.1%) of 28 cases (42.9%) and 1b in rest of the cases.

Keywords: hemodialysis, CKD, HbsAg, Anti HCV, Genotype 3b

INTRODUCTION

Hepatitis B (HBV) and Hepatitis C virus (HCV) infections are the commonest cause of viral Hepatitis among Hemodialysis (HD) patients.[1] Hemodialysis patients form the high risk population acquiring infections parentally, not only because of the large numbers of Blood transfusions they receive and invasive procedures they undergo, but also because of their immunosuppressed state.[2] As both the Hepatotropic viruses share common mode of transmission, co-infection between these two viruses are common, especially in areas where there is high prevalence of HCV infection and amidst people who are at high-risk for parenteral infection. [3]

Patients receiving maintenance hemodialysis (HD) are at a higher risk for acquiring Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) infections than the general population India,[4] contributes significantly to the global HCV burden. It is believed to harbour 12 - 18 million HCV-infected people.[5] The estimated prevalence of HCV in India is 0.5%– 1.5%,although variations may be seen across geographical regions.[4,5] The high level of prevalence have been related to several factors including, the duration of dialysis treatment, prolonged vascular access, the number of blood units and blood products transfused, organ transplantation, administration of drugs with contaminated syringes, occupational exposure to blood, and sexual transmission. [6] Present study was carried out to find out of the prevalence of viral markers like HBsAg and Anti HCV in the newly diagnosed Chronic Renal Failure patients, taken for maintenance Hemodialysis.

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MATERIAL AND METHODS

Present study was hospital based, prospective cross sectional and multicentered study, conducted in department of Microbiology, Department of Nephrology and Hemodialysis unit, Trichy SRM Medical College Hospital and Research Centre, Irungalur, Trichy, Tamilnadu., India. Study duration was of 1 year (January 2018 to December 2018). Study was approved by institutional ethical committee.

Inclusion criteria

- Patients of All age groups, both Genders, cases of Adult CKD taken for maintenance Haemodialysis, who had not received HBV vaccination at any point earlier, free from overt infection, immunosuppression & free from any chronic disease including autoimmune disorders, willing to participate in present study

Exclusion criteria

- Patients positive for HbsAg before haemodialysis.
- Patients positive for Anti HCV before haemodialysis.
- Patients undergoing haemodialysis for the first time.
- Patients who had underwent any surgical interventions
- Patients who had received Blood transfusion earlier.
- Patients on peritoneal dialysis (CAPD) only.
- Past history of sexual promiscuity.

Informed consent in vernacular was obtained from all the 1705 patients enrolled in this study. Patients who participated in this study attended the Hemodialysis centre twice or thrice weekly. Blood samples were collected from patients with Chronic Renal failure undergoing maintenance HD were tested for the presence of Hepatitis B surface antigen (HBsAg), and Anti HCV antibody by ELISA.

All the HCV seropositive samples were further confirmed by HCV RNA by Qualitative Real time Polymerase chain reaction and further studied for HCV Genotypes by RT PCR. All the 1705 serum samples were processed for HBsAg determination by HEPALISA (J Mitra) & for anti-HCV by HCV MICROLISA (J.MITRA).

All 1705 samples were further subjected for the following LFT,RFT, Hb estimation and Random blood sugar level. All the HCV Seropositive serum samples were confirmed by Real time RNA PCR (rt - PCR). Only HCV seropositive serum samples were further studied for genotypes by reverse transcriptase PCR by GeneXpert, Cepheid CE marked. This test was carried out in an outsourced and accredited laboratory with good quality control as per standards and the results were collected respectively.

Data was collected and compiled using Microsoft Excel,analysed using SPSS 23.0 version. Statistical analysis was done using descriptive statistics.

RESULTS

During this study period a total number of 1705 patients who satisfied the inclusion criteria,There were 1189 males (69.7%) and 516 were females.(30.3%) the age range of the study population was 22 to 82 years and their mean and median was 42.6 and 47 respectively.

TABLE 1: Distribution in relation to age and gender

Age group in years	Males	Females	total	Percentage
< 25	14	7	21	1.23
25 – 44	409	219	628	36.8
45-64	598	203	801	46.9
>65	168	87	255	14.9
Total	1189	516	1705	100

At the initiation of hemodialysis, among the study population two of them were reactive to HbsAg, 15 to anti HCV and five were found to be having co-infection. The prevalence of HbsAg and Anti HCV and both among the study was 0.11%, 0.87% and 0.29% respectively.

TABLE 2. Distribution of HbsAg and Anti HCV both prior to hemodialysis

CENTRE	TOTAL	HbsAg+ (%)	Anti HCV+ (%)	BOTH HbsAg& Anti HCV + (%)	BOTH HbsAg& Anti HCV - (%)
TOTAL (%)	n=1705	2 (0.11%)	15 (0.87%)	5 (0.29%)	1683

The distribution of HbsAg and Anti HCV among the healthy voluntary blood donors was 1.33% and 0.9% respectively. None of them carried both HbsAg and Anti HCV during the study period.

Table 3: Distribution of HbsAg and Anti HCV among the healthy volunteers:

Gender	Number	HbsAg positive	Anti HCV positive	Both positive	Both negative
Males	873	11	7	-	-

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Females	127	2	2	-	-
Total (%)	1000	13 (1.3%)	9(0.9%)	-	-

Comparison of distribution of HbsAg and Anti HCV among maintenance hemodialysis patients and healthy volunteers revealed that HbsAg was observed significantly more ($p<0.05$) among the healthy volunteers where there is no significant difference with regards to Anti HCV.

During the study period there were 93 drop out. There were 23 cases who were found to have either HbsAg or Anti HCV or both at the initiation of hemodialysis excluding these drop outs and positive viral markers, there were 1590 patients on maintenance hemodialysis at the e4nd of three months these 590 cases during a period of three months underwent a total of 4216 hemodialysis. These 1590 patients were screened for HbsAg and Anti HCV at the end of three months of hemodialysis, four of them showed seroconversion to HbsAg and eight of them were Anti HCV. Thus the seroconversion of HbsAg and Anti HCV was 0.25% and 0.5% respectively. None of them were seroconversion for both.

Table 4: Distribution showing seroconversion after three months of maintenance hemodialysis

Centre	Total at initiation	Total negative At initiation	Drop out	Total studied	HbsAg +	Anti HCV +	Both negative
Total (%)	1705	1683	93	1590	4(0.25%)	8(0.5%)	1578

Distribution of Hepatitis viral markers and gender in relation to gender when analyzed, 22 males and 12 females on MHD carried one or other viral markers or both viral markers. It appeared that the viral markers were more among males than females.

Table 5: Distribution of Hepatitis viral markers and gender

Virus	Male	Female	Total
HbsAg	5	1	6
Anti HCV	14	9	23
Both positive	3	2	5
Total (%)	22(64.7%)	12(35.3%)	34(100%)

Distribution of Genotypes of HCV virus during the study period revealed that 16 belonged 3b and the rest 12 belonged to 1b. Interestingly Centre 1 and 2 revealed only 1bwhereas Centre 3 and 4 revealed 1b and 3b. This genotypic study indicates that the prevalence of HCV genotype varies from Centre to Centre. HCV genotyping assay determined the Genotypes 1, 2,3,4,5 & 6 for the Anti HCV positive case, revealed that it belonged to genotype 3b.

Table 6: Distribution of HCV genotypes

Centre	HCV positive	HCV genotypes		
		1b	3b	mixed
Total (%)	28 (100%)	12 (48.9%)	16(57.1%)	-

DISCUSSION

Hepatitis B and Hepatitis C viral infections are one of the major health problems globally.[7] Chronic renal failure (CRF) patients, who are on hemodialysis, constitute a high risk of acquiring both parentally transmitted HBV and HCV infections.[8] There are various or multiple causes to acquire these infections and seroconversion when CKD patients were put on MHD. Hence this study was undertaken with the view of finding the prevalence and seroconversion of CKD on MHD.

628 were in the age group of 25 and 44, 801 in the age range of 45 to 64 and 255 were 65 years and above. Most of the CKD patients were at the age of 45 and above in this present observation that tallied with` the similar study of Abed El –kader Y El –Ottol*et al.*,[9] that showed the age range of 18-60 years with mean range of 44.5 years .

In the present study there was male preponderance. The ratio between male to female was 2:1. In most of the population male preponderance was noted in concordance with the study Khaled Z Badareen*et al.*,[10] that showed males were 61% and females were 39%. The male preponderance was due to health seeking behavior and preference was given to males by the existing social system.

Out of 252 HD patients, Diabetes mellitus 85 (33.7 %,) and hypertension 60 (23.8%) were the most common causes of renal failure. Similar to this study, a study by Hamzeh Al Zabadi*et al.*,[11] showed that Diabetes mellitus (35.4%) and Hypertension (25.8%) were the most common causes for renal failure.as Diabetes mellitus and hypertension are the metabolic disorders affecting mainly the kidney.

This study subjects who underwent HD for more than 5 years acquired greater risk of HCV infection, compared to patients with duration of HD less than three years which is similar to study Michael Jadoul *et*

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al.,[12]

Blood transfusion is cause for acquiring Hepatitis B and Hepatitis C viral infections was observed in earlier years befo0re the introduction of advanced screening tests for Hepatitis virus. Transmission of Hepatitis B and Hepatitis C viral infections was demonstrated earlier by similar to studies by Shiha AM *et al.*,[13] and Rajapurkar M *et al.*,[14]

Earlier studied demonstrated increased occurrence of seroconversion when CKD patients on HD moved from one center to another. This study was supported by Thompson *et al.*,[15] & Goodkin *et al.*,[16]. In the present study seroconversion was seen in the same center.

HBV vaccination has brought down the occurrence of HBV infection among CKD on MHD. Since CKD and HD is immunocompromised state, they need a greater number of doses as primary dose at 0, 1, 2 months and booster dose at 6 months than regular immunization schedule. In the present study seroconversion rate of HbsAg was 0.25% (4/1590). The occurrence would have been most likely that the patients would have been in incubation period of acquiring HBV infection. Similar observation were noticed by Akram *et al.*,[17] and Schneeberger *et al.*,[18] Prevalence of HBsAg in present study was in accordance with Mohammad Ali *et al.*,[19.]

Seroprevalence of anti HCV in present study was similar with other studies by Abed El-kader Y *et al.*,[9] and Khaled z Badreen*et al.*,[10] Prevalence of HBV and HCV among the hemodialysis patients were assessed and found to be 0.4% in HCV and nil in HBV. Itshowed variations with other studies,

In recent years there is a significant decrease in the prevalence of both HBV and HCV infections in industrialized countries. This decline is attributed, among other factors, like decrease in blood transfusions, administration of Erythropoietin, intensive vaccination against HBV and implementation of general biosecurity measures ,hand hygiene ,to prevent transmission of infection in hemodialysis units. Therefore, hospital infection control practices for the control of viral hepatitis must be introduced in all dialysis units.[20]

The present study of HD patients attending Centres 1,2,3,4 showed co-infection of HBsAg and Anti HCV as 0,0,0.64% AND 1.8% respectively. This is in concordance with studies by Edey M *et al.*,[21] Ghadir MR *et al.*,[20]

Both Hepatitis B virus and Hepatitis C virus share common mode of parenteral transmission .Both viruses can inhibit each other simultaneously; either virus can play a dominant role; both viruses have the ability to induce seroconversion of the other; the chronology of infection has a role in determining the dominant virus; and HBV and HCV can alternate their dominance.[11] However, the overall dominant effect appears to be HCV suppression of HBV. It is postulated that HBV coinfection in HCV-infected patients cannot be excluded by negative HBsAg status alone. Repeat PCR analysis might be required for the detection of HBV infection, especially in patients with HCV-related CLD.[12]

The present study showed that out of a total of 28706 study subjects, 26 patients were HCV Reactive, and most of the patients were3b (38.4%) followed by 1b (62%). This is in concordance with the studies by L.K.Silva*et al.*,[22] Simmonds P *et al.*,[23] and Fabrizzi F *et al.*,[24] as 61% & 39%, 59.8%, & 38.2%, 63% & 37% were 1b and 3b respectively.

An effective strategy to prevent nosocomial transmission of HBV and HCV in hemodialysis units to reduce the prevalence of infection should be implemented in strict compliance, with biosafety standards, measures of education, hygiene.

As our study showed, increased HCV prevalence than HBV we could conclude that the hepatitis C infection presents a high prevalence in patients undergoing dialysis and an anti-HCV test should be performed before being scheduled for hemodialysis Closed control of services should be given to HD patients such as blood transfusion and staff training to prevent the spread of this infection.

CONCLUSION

During the study period 1705 cases of CKD on MHD were screened. Male: female ratio among the study group was 2:1.Thereby indicating that there is male preponderance for MHD. The mean and median age patients undergoing MHD was 42.6 and 47 years respectively. Prevalence of HbsAg, Anti HCV and both among CKD at the initiation of MHD was 0.01, 0.87 and 0.29% respectively. The prevalence of HbsAg and Anti HCV among the healthy population was 1.3 and 0.9% respectively. Comparison of distribution of HbsAg and Anti HCV among MHD patients and healthy volunteers revealed that HbsAg was observed ($p<0.05$) among healthy volunteers, whereas there is no significant difference with regards to Anti HCV.

Seroconversion at the end of 3 months of MHD among the cases who were negative for HbsAg and Anti HCV was 0.25 and 0.5% respectively. Distribution of viral markers among healthy volunteers and HD population revealed that males were more affected compared to females irrespective of HbsAg or Anti HCV. Genotype 3b was identified in 16 (57.1%) of 28 cases (42.9%) and 1b in rest of the cases.

Conflict of Interest: None to declare
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