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ORIGINAL ARTICLE

PREVALENCE, SEROCONVERSION AND RISK FACTORS OF HEPATITIS B AND C INFECTION IN PATIENTS ON MAINTENANCE HEMODIALYSIS

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ABSTRACT: BACKGROUND: HBV and HCV infections pose a great threat to patients on hemodialysis and studies have been conducted regarding the prevalence and seroconversion rates. The present study was conducted to demonstrate the prevalence and seroconversion rate in patients with chronic hemodialysis and also the incidence of liver function derangement in patients with Hepatitis B and C.
METHODS: HBV and HCV status of patients who were on hemodialysis irrespective of serological status and etiology of renal failure were observed. 205 patients were followed up for a period of one year and the incidence, prevalence and seroconversion of HBV and HCV was estimated through HbsAg and Anti-HCV ELISA tests. T-test was used to compare different biochemical and other parameters among two groups (Reactive and Non-reactive). Linear regression was used to calculate the relationship between the parameters and seroconversion rates. **RESULTS:** 205 patients were observed in the study. The prevalence and seroconversion rates were 11.22% and 4.8% in HBV patients and 18.54% and 6.8% in HCV patients respectively, at the end of the study. There was a significant correlation of the prevalence with average number of blood transfusion and elevated ALT levels in HbsAg reactive patients. Additionally, anti-HCV reactive patients correlated significantly with average number of blood transfusion and elevated ALT levels. There was significant correlation with mean duration of haemodialysis and i.v drug abuse in anti-HCV reactive patients. Regarding the seroconversion status only the average number of blood transfusions was having a significant correlation in both HbsAg and anti-HCV reactive patients. **CONCLUSION:** The prevalence and seroconversion rates were 11.22% and 4.8% in HBV patients and 18.54% and 6.8% in HCV patients respectively. Safety can be improved with the availability of more sensitive tests, increasing use of erythropoietin, timely vaccination for hepatitis B and adopting universal precautions.
KEYWORDS: Hemodialysis, Hepatitis B, Hepatitis C, Prevalence, Seroconversion, Risk Factors, India.

INTRODUCTION: HBV and HCV infections are more frequent in patients on hemodialysis than in general population and are known to cause chronic liver disease.[1] Wide variations in prevalence of HBV and HCV infection in dialysis patients has been reported in different studies from India.[2] Study of seroconversion from negative to positive in HBV and HCV infection is an important method to access the efficacy of infection control measures in any dialysis unit. Various studies have shown that patients on long term hemodialysis are at increased risk of developing HBV and HCV infection.

Similarly hemodialysis was responsible for the high seroconversion rates.[3] Several other studies have revealed increased incidence of hepatic functional derangements in Hepatitis B and C infection in the form of elevated ALT and AST levels in patients on hemodialysis. The present study was designed to examine the prevalence of Hepatitis B and Hepatitis C in relation to duration of dialysis, to study the seroconversion from negative to positive in patients on chronic hemodialysis and to find out the incidence of liver function derangements in patients with Hepatitis B and Hepatitis C.

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PATIENTS AND METHODS: This was one year prospective study done in patients of End Stage Renal Disease (ESRD) on hemodialysis. All patients reporting to Nephrology Unit of a tertiary care Centre irrespective of serological status were screened for inclusion in the study. The patients who were on hemodialysis for a minimum period of 1 month and were likely to be available for follow-up for at least 6 months were included in the study. The patients who had acute renal failure were not included in the study. The patients were monitored for seroconversion every 3 months during their follow-up visits using HbsAg ELISA and Anti-HCV ELISA tests.

HBSAG ELISA TEST: The solid phase is made up of 12 strips of 8 polystyrene wells coated with the monoclonal antibody specific to HBsAg. During incubation, after serum or plasma sample is added along with a second antibody conjugated with horseradish peroxidase, an "Antibody-antigen-antibody sandwich immune complex" is formed and captured by the solid phase. If the sample tested contains the HBsAg, after washing and other treatment, the well turns yellow. Wells containing samples negative for HBsAg remain colorless.

ANTI-HCV ELISA TEST: Test kit is a solid phase enzyme immunoassay for the detection of antibodies to HCV in human serum or plasma. Serum or plasma samples are added to wells coated with HCV derived antigens. If antibodies specific for HCV are present in the sample, they form stable complexes with the HCV antigens attached to the well.

The microplate wells are washed and a goat anti-human immunoglobulin labelled with horseradish peroxidase is added. If the antigen/antibody complex is present, the peroxidase conjugate binds to the complex and remains in the well. After a second wash step, enzyme substrate is added. During incubation, a blue color develops in proportion to the amount of anti-HCV antibody bound to the well. Wells containing samples negative for anti-HCV antibody remain colorless.

RESULTS: Total 205 patients were observed at least for a period of 6 months for seroconversion. 159 patients were males (77.56%) and 46 were females (22.43%). Most common causes of end stage renal disease were diabetes mellitus (41%) followed by hypertension (25%). Out of total 205 patients, 23 patients (11.22%) were reactive to HBsAg ELISA test and 38 (18.54%) were reactive to anti-HCV ELISA test by the end of the study.

1 patient was both HBsAg reactive as well as anti-HCV reactive. 17 (73.9%) out of 23 HBsAg reactive patients received blood transfusions. 61 (33.5%) out of 182 HBsAg non-reactive patients received blood transfusions ($p<0.05$). Out of 38 anti-HCV reactive patients, 26 (68.42%) received blood transfusions. 52 (31.13%) out of 167 non-reactive patients received blood transfusions ($p<0.05$). Average number of transfusions received by HBsAg reactive patients (20.00) was significantly more as compared to non-reactive patients (12.75). Average number of blood transfusions received by anti-HCV reactive patients (22.80) was also significantly more as compared to non-reactive patients (10.02).

The average number of haemodialysis sessions done in HBsAg reactive patients was 66.73 as compared to 65.25 in non-reactive patients. There was no correlation between number of haemodialysis sessions and HBsAg reactive status ($p>0.05$). The average number of total haemodialysis sessions done in anti-HCV reactive patients was 109.63 and in non-reactive patients were 55.4. There was a significant positive correlation between average number of haemodialysis

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sessions and anti-HCV reactive status ($p<0.05$). The mean duration of haemodialysis in anti-HCV reactive patients (67.63 weeks) was significantly more than the mean duration of haemodialysis in non-reactive patients (43.5 weeks) (Table 1 & Figure 1).

10 patients (4.8%) who were initially non-reactive became HBsAg reactive during follow-up. 14 patients (6.8%) who were initially non-reactive became anti-HCV reactive during follow-up. Maximum number of patients underwent seroconversion between 6 months to 1 year after the start of haemodialysis. (Table 2 & Figure 2)

The average number of hemodialysis sessions in patients who seroconverted to HBsAg positive was 76.7+42.9.In patients who seroconverted to anti HCV positive this figure was 83.45+52.84. AST and ALT elevation was significantly higher in HBsAg reactive patients as compared to non-reactive patients. Only factor significantly contributing to seroconversion was number of blood transfusions. (Table 3 & Figure 3)

2 (8.69%) HBsAg reactive patients, had history of i.v. drug abuse while 11 (6.04%) HBsAg non-reactive patients, had history of i.v. drug abuse ($p>0.05$). Similarly 4 (10.5%) anti-HCV reactive patients had history of i.v. drug abuse while 9 anti-HCV nonreactive patients had history of i.v. drug abuse ($p<0.05$).

DISCUSSION: Hepatitis B and C infections continue to be a serious problem in chronic haemodialysis patients. This study was conducted to determine the prevalence and seroconversion characteristics of HBsAg and anti-HCV in patients with CRF, with the tests done at baseline and repeated after every 3 months. As it is observed from the results, the prevalence and seroconversion rates were 11.22% and 4.8% for HBV and 18.54% and 6.8% for HCV respectively.

The prevalence of HCV infection is known to vary widely in different regions of the world. In India, a very wide range of prevalence rates for HCV (4.3-45.2%) in the HD population has been reported.[4-9] Few recent studies from India have reported a prevalence rate of Hepatitis C as 4, 12.12 and 12.4 % whereas another recent study by Mittal et al reported a high rate of 30.5% at the end of study.[10-13] The reason for this variation in the prevalence rates of HCV among the HD patients is largely unknown.[12]

Though, implementation of universal precautions in hemodialysis units, blood transfusions, method used for virological testing of infused blood, reuse of dialyzers, method of testing HCV and variable isolation policies in different hemodialysis units could be the potential reasons for such variability. Prevalence rate of hepatitis C in our study was relatively higher as compared to few other studies from India.

Although we try to strictly follow universal precautions; lack of knowledge of nursing staff, not so good nurse to patient ratio and otherwise high prevalence of hepatitis C in general population could have contributed to relatively higher prevalence and seroconversion of hepatitis C in our study. Moreover, we have only recently started testing blood products by NAT (nucleic acid test) and non-detection of hepatitis C virus in blood products in earlier part of study could have contributed to a relatively higher prevalence and seroconversion.

Several studies from developed countries have shown HBsAg prevalence rates to range from 4% to 15% in HD patients.[14,15] In India, HBV prevalence in HD patients ranged from 3.4% to 45% which is clearly in excess to the prevalence of 4.7% in the general population.[16] In a recent study conducted by Bhowmik et al in hemodialysis patients, new hepatitis B infection was found in 5.5 %.[11]

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HBV is less prevalent than HCV in HD units because of HBV vaccination, isolation of HBV positive patients, use of dedicated dialysis machines and regular surveillance.[13]

Prevalence of hepatitis B was relatively higher in our study. Our centre is a tertiary care hospital in northern India catering patients across three states. So, we receive patients with multiple comorbidities and these patients are likely to have multiple infections including hepatitis. Moreover, we receive patients at a relatively later stage of CKD and effectivity of hepatitis B vaccination decreases as renal function declines, making patients prone to hepatitis B infection in spite of vaccination.

Seroconversion of hepatitis B and C in our study was 4.8 and 6.8 % respectively. In a recent study conducted by Kumar et al seroconversion rates for hepatitis C have been reported as 7.44% where as a high seroconversion rate of 14.4 % was reported in a study conducted by Mittal et al. [12,13] Kosaraju et al in their study reported a very low prevalence and seroconversion rate of hepatitis B and C.[17] Similarly, we also found a low seroconversion rate of hepatitis C (4.8%) at our dialysis centre.

Relatively high seroconversion rate of hepatitis B at our centre was probably due to the fact that our centre is a tertiary care referral centre and offers maintenance hemodialysis as well. Many patients coming to our centre do not reveal the very fact that they are receiving/have received hemodialysis sessions at other centers. Centers located in smaller cities many a times have one or two hemodialysis machines and do not strictly follow isolation policies.

Duration of hemodialysis and number of hemodialysis sessions were significant contributing factors towards development of hepatitis C infection whereas it was not so with hepatitis B.Most studies state that longer duration of dialysis is related to a positive anti-HCV rate [4, 18, 19]. A recent study by Kosaraju et al highlights the duration of dialysis as an important risk factor for infection among haemodialysis patients.[17] This observation was in agreement with previous reports in Palestine, Moldavia, and other studies from different regions of the world.[20–23]

Duration of dialysis is an important risk factor for acquiring infections as it is related to nosocomial transmission and dissemination of the infections in the dialysis units.[17] While analyzing patients who seroconverted, number of blood transfusions received significantly contributed to development of either hepatitis B or C infection in our study. Several studies have shown that the risk of acquiring the HCV infection increased with an increase in the number of units of blood which were transfused.[18,24,25]

Our study had several limitations. First, we did not use HCV RNA for testing of hepatitis C due to financial constraints, which is now the recommended test in hemodialysis population in areas of high prevalence. Secondly, we did not analyze data regarding patients receiving dialysis at other centers and its contribution to seroconversion.

Thirdly, we did not evaluate efficacy of hepatitis b vaccine in our patients and whether a relatively higher rate of seroconversion was due to inadequate antibody titres. Nevertheless, our study emphasizes need to adopt strict universal precautions, use of erythropoietin to reduce number of blood transfusions and use of vaccination to limit the prevalence and seroconversion of hepatitis in hemodialysis population.

CONCLUSION: The prevalence and seroconversion rates were 11.22% and 4.8% in HBV patients and 18.54% and 6.8% in HCV patients respectively. Number of blood transfusions significantly contributed to development of either hepatitis B or C whereas number and duration of haemodialysis

and history of is drug were other significant risk factors for acquiring Hepatitis C in CRF patients on regular hemodialysis.

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Parameters	HbsAg Reactive		HbsAg Non-reactive		Anti-HCV Reactive		Anti-HCV Non-reactive	
Number of haemodialysis	66.73±52.97		65.25±114.12		109.63+106.08*		55.4+51.12	
Mean duration of haemodialysis	49.04±19.31		47.75±51.72		67.63+48.99*		43.50+32.7	
Patients with blood transfusions	17 (73.9%)*		61 (33.5%)		26 (68.42%)*		52 (31.13%)	
Mean number of blood transfusion	20.00±12.07*		12.75±15.06		22.8+18.19*		10.02+10.34	
Patients with i.v drug abuse	2 (8.69%)		11 (6.04%)		4 (10.5%)*		9 (5.38%)	
Patients with history of jaundice	4 (17.39%)		19 (10.40%)		9 (23.68%)		14 (08.38%)	
AST	**Elevated**	**Normal**	**Elevated**	**Normal**	**Elevated**	**Normal**	**Elevated**	**Normal**
	11 (47.8%)*	12 (52.17%)	35 (23.64%)	113 (76.35%)	15 (39.47%)	23 (60.52%)	31 (23.13%)	103 (76.86%)
ALT	13 (56.52%)*	10 (43.47%)	34 (22.97%)	114 (77.02%)	20 (52.63%)*	18 (47.63%)	27 (20.14%)	107 (79.85%)

Table 1: Relation of prevalence with various parameters in HBV and HCV positive patients

* Indicates significant values that is < 0.05

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Patient Status	Prevalence	Seroconversion
HbsAg reactive	23 (11.22%)	10 (4.8%)
HbsAg non-reactive	182 (88.78%)	-----
Anti-HCV reactive	38 (18.54%)	14 (6.8%)
Anti-HCV non-reactive	167 (81.46%)	-----

Table 2: Prevalence and seroconversion rates in HBV and HCV patients

Parameters	Patients who seroconverted to HbsAg reactive		Patients who seroconverted to Anti-HCV reactive	
Mean number of hemodialysis	76.7±42.9		83.45+52.84	
Mean duration of hemodialysis (weeks)	52.1±41.49		63.57+39.59	
Patients with blood transfusions	8 (80%)*		12 (85.71%)*	
Mean number of blood transfusion	22.62±10.69*		26.08+11.38*	
AST	**Elevated**	**Normal**	**Elevated**	**Normal**
	2 (20%)	8	4 (28.57%)	10
ALT	3 (30%)	7	6 (42.85%)	8

Table 3: Showing the relation of seroconversion status with various parameters in HBV and HCV patients

* Indicates significant values that is < 0.05

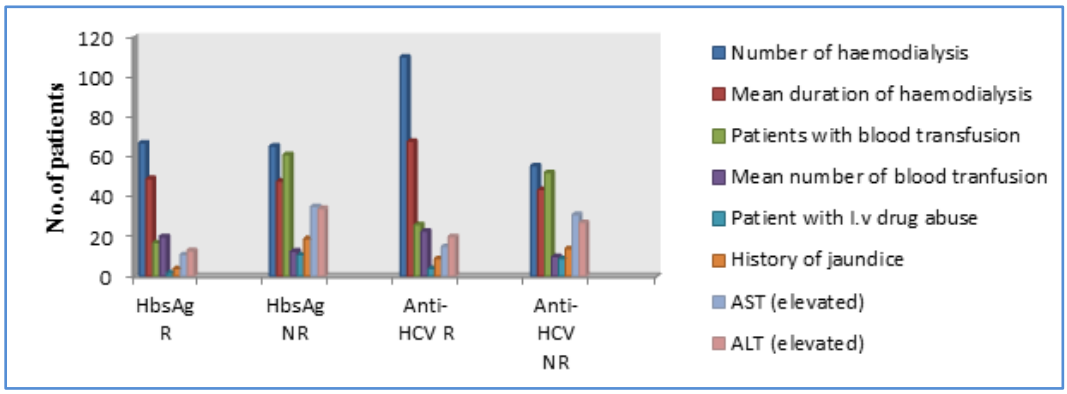

Fig. 1: Relationship of prevalence with various parameters in HBV and HCV patients

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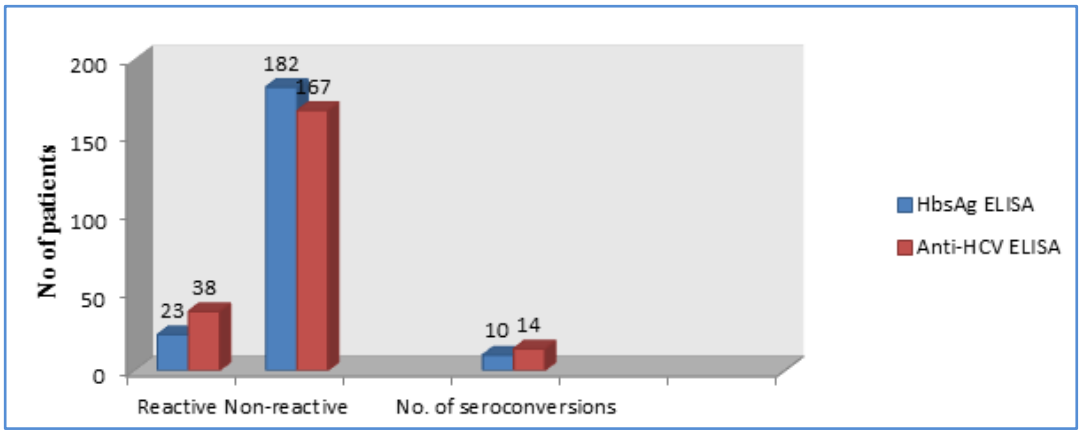

Fig. 2: Prevalence and seroconversion rates in HBV and HCV patients

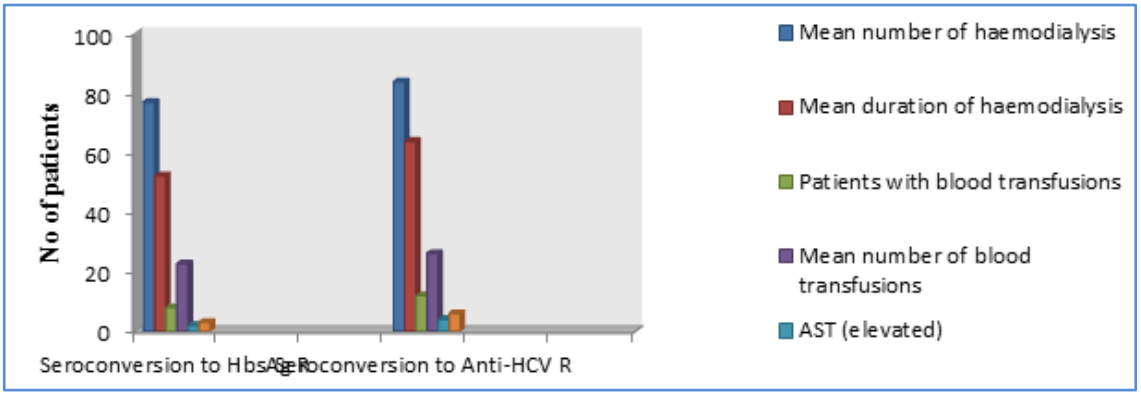

Fig. 3: Relationship of seroconversion status with various parameters in HBV and HCV patients

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