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Prevalence of transfusion transmitted infections in children with inherited coagulation disorders

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ABSTRACT

Background: Factor replacement and blood product transfusion are the main stay of treatment of inherited coagulation disorders. Even though interventions with these products have led to the decrease in morbidity and mortality of these patients, repeated use of these products especially before 1980s where the viral inactivation of factors and blood bank screening methods were not stringent, have led to the occurrence of transfusion transmitted diseases in haemophiliacs especially hepatitis C infection.

Methods: 50 children including adolescents under the age of 18 years with inherited coagulation disorders were screened for hepatitis B and C infection during 2 medical camps conducted at an interval of 6 months, blood samples and medical information were collected prospectively during these periods. The blood samples were tested for surrogate marker for hepatitis B and anti HCV using enzyme immunoassay.

Results: All the children screened were negative for hepatitis B and C markers.

Conclusions: The incidence of post transfusion hepatitis has dramatically decreased following stringent blood donor screening methods as well as availability of purified and recombinant factors. The current risk of transfusion transmitted infections in these patients are very low almost comparable with general population.

Keywords: Disorders, Hepatitis B, Hepatitis C, Inherited

INTRODUCTION

Inherited bleeding disorders constitute a spectrum of diseases in which there is a primary defect in haemostasis and deficiency of coagulation factors. ^{1,2} This entity comprises of haemophilia A and B (95%), other rare clotting factor deficiencies and Von Willibrands disease. Because of high prevalence of consanguineous marriage, the countries like middle eastern countries and southern India harbour more number of these X-linked and autosomal recessive disorders.³

Even though, the first treatment for haemophilia was reported in 1840, fractionation of human plasma was developed only one decade later in response to the challenges of the second world war.^{4,5} The life of people with haemophilia was revolutionised by the development of cryoprecipitate. During the 1970s human freeze-dried (lyophilised) FVIII and FIX became available which even lead to home therapy. Plasma derived products were prepared from donor pool size, which could even be between 10,000 and 20,000. Such products were not heated until 1985. The availability of these products resulted in a dramatic improvement in treatment.⁶

Treatment of hemophiliacs with human factor VIII concentrate similarly carries a risk of hepatitis.⁷ There is a higher incidence of hepatitis in patients receiving transfusions of blood obtained from paid donors compared with patients whose transfusions were obtained

from volunteer donors.⁸ The early concentrates were not subjected to a viral inactivation.⁹ Procedure during preparation and their use was associated with a high prevalence of non-A, non-B (NANB) hepatitis.¹⁰

Hepatitis C (HCV) is caused by an RNA virus of the flaviviridae family. Hepatitis C is a disease with varying rates of progression. HCV is a blood born pathogen and is predominantly spread via exposure to contaminated blood or blood products. The incubation period on the average ranges from 2 to 7 weeks. Each year 30,000 new cases are being diagnosed.¹¹ Prevalence is highest among groups with specific risk factors especially drug users by injection and patient with hemophilia or those on long term hemodialysis and also people who have received blood or organ product prior to June 1992. Prevalence of HBV and HCV in India is about 1-5% and 1% respectively.¹² Hepatitis C virus infection appears to be endemic in most parts of the world with prevalence of 3%.13,14 Haemophilia patients who are younger and are frequently co-infected with human immunodeficiency virus would have higher risk of cirrhosis (37%), hepatocellular carcinoma (12%) and liver related death (19%).¹⁵ Transfusion transmitted diseases are a major cause of morbidity and mortality in haemophiliacs who received non virucidally treated large pool clotting factor concentrates before 1986.

Chronic Hepatitis B infection is determined by finding HBV DNA and usually HBeAg in the serum. Many with chronic infection develop chronic liver disease with histological changes and elevated liver enzymes. Chronic liver disease can progress to cirrhosis. The commonest form of hepatitis following factor VIII transfusion is reported to be HCV infection. The aim of the present study was to observe the prevalence of hepatitis B and C infection among patients with inherited coagulation disorders of age less than 18 years attending a screening camp of Pariyaram Medical college

METHODS

Study was conducted 50 patients with coagulation disorders requiring multiple episodes of factor replacement as well as blood product transfusions, in a screening camp conducted in Pariyaram Medical College in north Kerala. Total of 50 patients were interviewed according to the inclusion criteria by a pre-tested questionnaire and screening test for HbsAg and Anti HCV was conducted. Consent was taken from parents before conducting the interview.

Blood samples were collected by finger prick technique using all aseptic precautions. HbsAg and anti HCV was tested using kits provided by Bhat Bio Tech India Pvt Ltd

Hepa Scan HbsAg rapid strip test kit used. The test is a rapid, qualitative, one-step immunoassay based on the immunochromatographic principle. This method employs unique combination of monoclonal dye conjugate

(colloidal gold) and polyclonal solid phase antibodies to selectively identify Hepatitis B surface antigen with a high degree of sensitivity. Monoclonal antibody is conjugated with colloidal gold and is impregnated at the sample pad. The polyclonal antibodies are selectively immobilized at the test band area. On dipping Dipstick in the Specimen, the test sample flows through the sample pad by capillary action. If the serum contains HBsAg it will form a complex with antiHBsAg colloidal gold conjugate and allows this to be trapped by the test line, causing the formation of a red line. The unbound colloidal gold particles continue to move along the strip by capillary action until they come in contact with the control.

HEPASCAN Hepatitis C Virus card test is an immuno chromatography-based assay for the qualitative detection of Hepatitis C virus in human serum/plasma/. HCV Card test is indigenously developed rapid test device to qualitatively detect the presence of antibody to HCV in whole blood/serum or plasma specimens. This is only screening test for detection of HCV antibodies. If the sample gives positive result in this method confirmatory tests such as ELISA, Immuno Blot should be performed. This test is based on immuno - chromatographic principle. The test device consists of sample window containing a reagent release pad. The reagent release pad is held in contact with the porous membrane material. The membrane has three zones. The first zone is mobilized by the sample and it consists of coloured colloidal gold particles sensitized with protein A. The second zone consists of recombinant HCV antigens immobilized on the membrane (Test line). The recombinant HCV antigens used in this test include both structural (nucleocapsid) and nonstructural protein including NS-3, NS-4 and NS-5. The third zone (Control line) consists of control antibody, which is also immobilized on the membrane. If HCV antibody is present in the test sample, it will form a complex with the protein A - collodial gold conjugate and then move on, to be trapped by the test line, causing the formation of red line. The unbound colloidal gold particles continue to move along the strip by capillary action until they come in contact with the control line and are trapped, giving a red line demonstrating the validity of the test.

RESULTS

The study was conducted at haematology clinic at Pariyaram Medical College and all patients with coagulation disorders registered under Haemophilia society under the age of 18 years. Following are the results of the study:

Average age of the patient population was 10.54 ranging from 2 years to 18 years. 94% (47) of the study population was males and 6% (3) were females. Average amount of units of factor used by a patient per month was found to 490.4 Units (range:0-2400). Frequency of usage of Factor per month is on an average 1.26 (Range: 0-6).

Total number of treatment by factor taken per year by an individual patient is 11.18 times (Range:0-50). Total of 13(26%) patients out of 50 had history of previous surgical procedures and 12(24%) had past history of various dental procedures. 2 out of 50 (4%) reported to have had high risk sexual behavior.

Table 1: Profile of inherited coagulation disorders.

Type of disorder	Number of patients	%
Haemophilia A	36	72
Haemophilia B	8	14
Von Willibrands disease	2	4
Factor 7 deficiency	0	0
Others	4	8

The study population was all born after 1990 and had started their treatment in post-1990 era. Majority (50%) are under the category who have taken both NHT factor and various blood products. In the study population 4 out of 50(8%) have taken factor prophylaxis as per protocol at various point of life whereas majority (92%) did not take factor prophylaxis.

Table 2: Treatment details of patients with inherited coagulation disorders.

Treatment	Mean	Standard deviation	Minimum	Max
Units per month	490.4	511.91	00	2400
Frequency per month	1.26	1.55	00	6.00
Frequency per year	11.18	13.21	00	50

72% of study population had taken Hepatitis B vaccination.90% of these patients were doing the screening test for hepatitis B and C for the first time. 10% of them were screened for these infections previously and were found to be negative.

Table 3: Type of blood component.

Type of therapy	Number of patients	Percentage
Fresh frozen plasma	1	2
FFP/Cryo/whole blood	8	16
Intermediate purity factor	6	12
NHT factor+blood product:	25	50
Purified factor	10	20

HIV status was not known or tested in 72% of the patients and 28% were tested previously for HIV status and were found to be negative.

None of the study population was found to be having Hepatitis B or C positivity irrespective of the type of

blood products taken and amount of factor treatment taken.

DISCUSSION

In a study in western India by Gosh and etal in 2000 on patients with haemophilia, it is found to be positivity of HIV 3.8% and 6 % for hepatitis B and 23.9 % for HCV. 17 Present study even shows much better results, probably due to better screening facility for blood banks in south India and advances in the screening tests especially for hepatitis C. We didn't conduct HIV screening in these patients. A longitudinal study of 44 haemophilics children by G Nebbia and G.A Moroni, all treated with factor concentrates, 24 (55%) showed signs of hepatitis B infection, while 20 (45%) did not. Age at onset of treatment, number of infusions and total amount of concentrate used did not show significant correlation. Early age of infection is an important factor in predicting chronicity.¹⁸ It was found that 41 of the patients, had raised ALT, of which 35 were those who along with raised ALT were also HCV antibody positive in present study the 100% of children were found to be both hepatitis B and C negative, despite of the fact that some of these children were treated with blood products and plasma derived factors. This may be due to the stringent precautions taken by blood banks in Kerala.

The prevalence of HCV in blood donors varies from country to country and population to population. Western countries have a prevalence rate of 0.4% or less, it is relatively higher in Japan at 1.4% and significantly higher in third world countries.¹⁹ A study on healthy blood donors from AKUH reported that 1.18% of donors were positive for anti HCV.²⁰ Another study in this city conducted on professional donors showed a very high rate of seropositivity i.e. 20.7%.21 Hepatitis C antibody is relatively an expensive test. Alternatively raised ALT was tested whether it can serve as a surrogate marker for hepatitis in haemophilic patients or not. Total of 124 Indian patients with haemophilia and 185 multiple patients transfused with thalassaemia, haemoglobinopathies, patients on chronic haemodialysis and others were screened for HIV-1 infection by a commercially available competitive ELISA test and supplementary Western Blot (WB) test. The results showed that HIV-1 infection was mostly confined to the haemophiliacs where 15 (12.1%) were confirmed to be positive for HIV infection.²² In a study on HCV status on post cardiac surgery patients by James Donahue and etal the incidence of infection was found to be the risk of HCV seroconversion per unit transfused was 0.19 percent.²³ In a study by Karimi etal in southern Iran in none of the patients were immunodeficiency virus positive but 47 (15%) were hepatitis C virus positive and two (0.7%) were hepatitis B positive, so that the rate of transfusion-transmitted infections was lower compared with other populations.²⁴ In a study by Katayoun Samimi in patients with inherited bleeding disorders 98.3% were found to be Hepaitis B

negative almost comparable to present study.²⁵ In a study done in Pakistan in 2017 anti HCV antibody was positive in 18% and HBsAg was positive in 3% of patients.²⁶

Bloodborne viral infections are another potential complication of treatment in haemophiliacs. Hemophiliacs have many risk factors that are associated with hepatitis infections, including age; disease severity; the use of factor concentrate versus cryoprecipitate or designated donor replacement therapy, type, amount of concentrate used and the virucidal treatment procedures that the concentrate has undergone.²⁶

Transfusion-transmitted infections is a serious public health problem in haemophiliacs who repeatedly receive blood products and plasma derived factors. It is usually resultant from poor blood screening practices. Economic resource constraints are a major hurdle in the management of haemophilia. Most of the patients get treated with blood product transfusions mostly before proper diagnosis and plasma derived factors after wards. NHT factors transfusion changed the outcome of haemophiliacs with regard to TTI . This study as it includes patients less than 18 years only, the treatment modality was mainly by NHT factors (50%) and some patients requiring blood products In present study, we have found the overall prevalence of HCV as zero compared which is lesser than 8% previously reported amongst the general community of Pakistan.²⁷ Prevalence study of viral hepatitis in a large US hemophilic population showed that active infection with HCV is common, occurring in 89% of all study patients regardless of HIV status.28

The main change in the whole prevalence might be due to use of tertiary level treatment of factors which even removes the non-lipid soluble viruses and better health facilities in Kerala. Overall prevalence of TTI was 0.6% with a higher prevalence in replacement donors and male donors.²⁹ The general prevalence of HCV is less in our area and the absence of HCV and HBSAg in our population also may be due to increased percentage of children who get vaccinated against hepatitis B.

CONCLUSION

Countries with a greater HCV prevalence in the general population had a greater prevalence level of the infection in multiple transfused patients. Compared to other nations India has comparatively low prevalence rate of HCV. But still, standard screening approaches are accessible only in few blood transfusion centers of large cities. Transfusion transmitted infections can be minimised to a great extent by educating people and creating awareness among the public. Immunisation of the succesptible population with hepatitis B can decrease the chances of these infections. The facilities for screening tests for Hepatitis B virus, Hepatitis C virus, and Human immunodeficiency virus would be available in all health care and transfusion centers. Stringent

methods should be implemented for donor selection. Safety injection practises should be followed along with good quality services at the blood banks can reduce the prevalence of TTI to a significant extent. The limitation of the present was that HIV patients could not be screened.

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Institutional Ethics Committee

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