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Follow up of Hepatitis B and Hepatitis C positive blood donors –A study

Pathology

KEYWORDS: Hepatitis B,Hepatitis C,donors, NGO, HBe Ag,

Dr. Rima Kamat (MD Pathology)Professor(Additional), Dept. of Pathology, TN Medical College and BYL Nair Charitable Hospital, Mumbai.

Dr Jyothi.B.Shetty (MD Pathology)Assistant Professor, Dept. of Pathology, TN Medical College and BYL Nair Charitable Hospital, Mumbai.

Dr Priya Chikhalikar (MD Pathology)Ex Senior resident, Dept. of Pathology, TN Medical College and BYL Nair Charitable Hospital, Mumbai.

ABSTRACT

Background: Hepatitis B virus is one of the most important causes for chronic viral hepatitis. Chronic infection with Hepatitis C virus can manifest from being an asymptomatic carrier to chronic liver disease which may lead to chonic hepatitis,liver cirrhosis and hepatocellular carcinoma. This study was carried out with the aim of increasing awareness of hepatitis in blood donors ,increasing rate of early detection,proper counselling and follow up of the donors who tested positive either for HBV or HCV in pretransfusion screening.

Materials and Methods: This study was carried out in a FDA approved blood bank of a tertiary care hospital over a period of three years(August 2009-August 2012).All healthy asymptomatic blood donors from indoor and outdoor blood collections who on routine pretransfusion screening tested positive for Hepatitis B and Hepatitis C viruses were included in the study.These donors were informed about their serological status and referred to a NGO which works for the benefit of Hepatitis B and C positive blood donors.This NGO confirmed the diagnosis,counselled them to follow up of donors with their spouses and family members.

Results: Overall seroprevalence of Hepatitis B was more in replacement donors compared to voluntary donors. Total 76 HBsAg positive donors followed with the NGO ,of these 8 were HBeAg positive chronic hepatitis B.Of the remaining 68 HBeAg negative donors,3 had HBV DNA levels >1,00,000/ml and elevated alanine aminotransferase levels.These were HBeAg negative chronic Hepatitis B patients.One HBeAg positive donor underwent treatment with interferon alpha.10 out of 36 HCV positive donors followed up with the NGO,of which 4 tested positive for HCV RNA genotype ,3 for genotype 3 and one for genotype 1.

Conclusion: Healthcare professionals,NGO's and Government agencies should strive to increase the awareness of transmissible diseases and increase the rate of early detection and regular follow-ups for the benefit of the community.

Introduction

Transfusion of blood and blood components as a specialized modality of patient management saves millions of lives world wide and reduces morbidity. Blood transfusion is associated with a large number of complications, some trivial &others life threatening demanding for meticulous pretransfusion screening particularly for Transfusion Transmissible Infections(TTI).[1,2]Infections caused by Hepatitis B virus(HBV),Hepatitis C virus(HCV) and Human Immunodeficiency Virus(HIV) remain the most important health problems in transfusion of blood & blood products worldwide. So screening of blood for detection of TTIs namely HIV,Hepatitis B,Hepatitis C,syphilis and malaria is mandatory under the Drug and Cosmetic Act,1945(amended from time to time)by Ministry of Health & Family Welfare, Government of India.[3]

Hepatitis B is one of the most frequent causes of chronic viral hepatitis worldwide. Approximately at least 2 billion people have had contact with the virus and more than 400 million people are chronic carriers.[4,5]The seroprevalence of Hepatitis B in the world varies from 0.1% to 20%,being highly endemic in all of Africa, some parts of South America, eastern Europe, south east Asia, China & Pacific Islands except Australia, New Zealand & Japan.[6,]The chronic liver disease and Hepatocellular carcinoma(HCC) associated with HBV infections are among the most important human health problems in high prevalence regions. Despite the low incidence of disease seen in general population ,certain groups who are sexually promiscuous or who have frequent contact with blood or blood products have a high rate of HBV infection.[7] The global prevalence of HCV is around 2% with 170 million persons chronically infected with the virus .The prevalence of Hepatitis C is higher in some countries in Africa and Asia . [8]

There are many Non Governmental Organizations(NGOs) working for benefit of patients tested positive for Hepatitis B and Hepatitis C virus infection. A project was started jointly by a NGO and Federation of Blood Banks in a metropolis to increase awareness and rate of early detection of Hepatitis B and Hepatitis C, proper counselling and follow up of blood donors who tested positive either for Hepatitis B or Hepatitis C.

With this aim the present study was carried out in a FDA approved blood bank of a tertiary care hospital over a period of three years in asymptomatic healthy voluntary blood donors.The donors were followed up with the help of NGO with proper speciality guidance; follow up with blood tests and screening and vaccination of family members when required.

Materials and Methods

The present study was conducted in a FDA approved blood bank of a tertiary care hospital over a duration of three years. The sample size was 100-120.All healthy asymptomatic blood donors from indoor and outdoor blood collection units who on routine pretransfusion screening tested positive for Hepatitis B and Hepatitis C viruses were included in this study.

After following FDA donor selection criteria and taking consent for blood donation ,blood was collected under strict aseptic precautions. The samples were properly labelled and they were subjected to a battery of serological tests for detection of HIV, Hepatitis B, Hepatitis C virus and syphilis. Indirect ELISA kits of third generation were used for detection of Hepatitis C and direct ELISA (Sandwich ELISA)for Hepatitis B virus.

The donors who tested positive for either Hepatitis B or Hepatitis C were informed about their serological status by sending letters in three different languages ,i.e English ,Hindi and regional language.In case of no response from them reminder phone calls were made by the social workers.Those who responded were counselled in the blood bank .The information about the nature of the disease,modes of transmission,course of the disease,importance of timely intervention and proper follow up was emphasized on them.Blood sample was again collected for confirmation and when donor came to collect this report he was informed about the NGO which worked for the benefit of Hepatitis B and Hepatitis C positive donors.

A joint venture had been started by this NGO and the Federation of Blood Banks with the aim of developing new operational approaches that can be incorporated into health and social practices for blood donors on a nationwide basis.This NGO confirmed the diagnosis ,counselled the donors and their partners who followed up.HBV vaccination was offered where appropriate.

Details of these donors with their followup investigations and treatment with the NGO were collected over the study period to find out the disease status in these donors.

Simple analytical tests were used for analysis of this data.

Results:

The study was carried out in a tertiary care hospital FDA approved blood bank over a period of 3 years i.e from August 2009-August 2012.All blood donors of outdoor blood donation camps and indoor collection units were included in the study.A total of 47,269 blood donors donated blood in these 3 yrs.Yearwise total blood collection during study period is shown in Table 1.

Highest blood collection was observed in the year August 2010 to July 2011.Among the total 47,269 donors ,majority of the donors i.e 39,428 donors(83.41%) were voluntary and remaining 7,841(16.59%) were replacement donors.There was a dominance of male donors contributing to about 43,565 donors(92.16%) of the total donors over the period of three years.Female donors were 3,704 (7.84%).The prevalence of HBsAg positive and HCV positive blood donors remained same during the study period.(Table 2)

Majority of positive blood donors were in the age group of 18-38 yrs for both HBsAg and HCV i.e 84.96% and 83.25% respectively.

The overall seroprevalence of hepatitis B in replacement donors was higher (1.52%) as compared to voluntary donors (1.10%) and the difference was found to be significant($p<0.05$).However though the incidence of Hepatitis C during this period was more in replacement donors(0.28%) than in voluntary donors (0.19%),the difference was not statistically significant($p>0.05$). (Table 3)

The average follow up of Hepatitis B positive blood donors was 13.77% and that of Hepatitis C positive blood donors was 37.5% during the study period.Highest follow up of both Hepatitis B and Hepatitis C was seen in the last year of the study as seen in Table 4.

On follow up the common positive history given by Hepatitis B and Hepatitis C positive donors (34.82%) was past history of jaundice (more than a year back).The other positive history given was surgery/dental work(23.21%),alcoholism(22.32%), & blood transfusion(8.93%).12 positive donors(10.72%) did not have any positive history.Of the total 76 HBsAg positive donors followed with the NGO, 8 were HBeAg chronic hepatitis B (10.53%). 3 (3.95%)of the 68 HBeAg negative donors had HBV DNA levels >1,00,000/mL and had elevated alanine aminotransferase levels. These were HBeAg negative chronic Hepatitis B patients. 65.(85.52%) of them were HBeAg negative chronic inactive carriers (Fig 5).One of the HBeAg positive donor underwent treatment with interferon alpha.

Fig 6 shows the HCV RNA status in HCV positive donors.Of the 10 (27.78%) who were HCV RNA positive,4 tested positive for HCV RNA Genotype ,3 were positive for Genotype 3 and one for Genotype 1.

Discussion:

The present study was carried out with the aim of early detection of Hepatitis B and Hepatitis C positive healthy voluntary blood donors and their follow up.There is an increasing incidence of Hepatitis B and Hepatitis C infection especially in developing countries like India causing an increasing burden of carriers.These healthy carriers if undetected pose a threat to the community,

Our study showed predominance of voluntary donors(83.41%) as shown in Table 3.This finding was comparable to the study carried out by Patel et al(2012) in a Secondary Care Hospital over 7years in Ahmedabad where voluntary donors accounted for 95.56% of total donors.[9]In contrast predominance of replacement donors was found in a study by Arora et al at a blood transfusion centre of a Medical College in Haryana where 68.6% were replacement donors and 31.4% were voluntary donors.[10]This reflected lack of awareness and motivation about blood donation, misconceptions and fears associated with blood donation and indifferent attitude of the health sector in the particular community. A large scale multidisciplinary approach towards enhancement of voluntary donations needs to be undertaken by the Government of India.[11] In the present study the predominance of voluntary donors could be due to the large number of outdoor camps organized by social workers creating public awareness and the study being carried out in a metropolis.

A predominance of male donors (92.16%) was seen in this study.The observation was similar to study done by Singh et al(2009) in coastal Karnataka.[12] The various reasons for male predominance in our study could be social taboo, fear of blood donation and deferral of female donors of reproductive age groups due to reasons like anemia, pregnancy, and breast feeding. Incidence of Hepatitis B among blood donors in our study was found to be 1.17%.(Table 2) Patel et al in their study reported Hepatitis B prevalence of 0.30%.This low seroprevalence was attributed to inability to detect the disease in pre-seroconversion or window phase of the infection,high cost of screening,lack of funds and trained personnel,immunologically variant viruses and non-seroconverting or immune silent carriers.[9]Kaur et al (2010) in their study over a period of 5 years in Chandigarh reported prevalence of HBV positive donors to be 1.7%.[13]

The number of HCV positive donors in our study was 96 out of a total of 47,269 donors accounting for 0.20% of total donors.(Table 2)Tessema et al (2010) carried out a four year study in Ethiopia in a tertiary care hospital in which 6,361 donors were screened and 0.7% were positive for Hepatitis C infection.[14]According to Mukhopadhyaya(2008) most of the studies in India for the prevalence of Hepatitis C were carried out in blood banks with the assumption that blood donors are surrogate for population at large.[8]Most of the studies note a prevalence of Hepatitis C below 2%.The high prevalence in professional blood donors calls for need of stringent donor screening criterias.[12] Although the incidence of Hepatitis C infection has dramatically decreased during the past decade ,the worldwide reservoir of clinically infected person is estimated at 170 million ,or 3% of the global population.[15]

In our study there was difference in prevalence of seropositivity of Hepatitis B in voluntary and replacement donors. There was decreasing trend in the prevalence of Hepatitis B in voluntary donors with 1.21%, 1.07% and 1.02% in the three years of study respectively.Opposed to this an increase in prevalence(1.82%) was observed in replacement donors in the third year compared to the first two years(Table 3).The difference in seropositivity in voluntary and replacement donors was found to be significant($p<0.05$).This finding was similar to the observation made by Kaur et al where the prevalence of Hepatitis B was 0.65% in voluntary donors and 1.07% in replacement donors.The high seropositivity in replacement donors could be due to number of factors like concealing high risk behavior and paid donors posing as relatives.[13]

Similar difference was observed in seroprevalence of Hepatitis C in voluntary and replacement donors.(Table 3)However the difference was not significant($p>0.05$%).Similar observation was made by Garg et al in their study where all their HCV positive donors were replacement donors.[16]

All the HBsAg and HCV positive donors in our study were contacted by our blood bank personnel keeping their serostatus confidential. Correspondence letters were sent and if they didnt respond within a week, telephonic calls were made.On their arrival in blood bank they were counseled about their disease and informed about the nature

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and modes of transmission of the disease.They were advised to avoid blood donation.They were informed about a voluntary organization which works for the benefit of Hepatitis B and Hepatitis C positive patients and that it offers special counseling and free follow up with viral markers ,HBV DNA and HCV RNA levels.Investigations like liver biopsy and ultrasonography were done if indicated and treatment given if required .Family members were also screened and vaccination given if found negative.The donors were motivated to follow up with this organization.On an average only 13.77% of total HBsAg positive donors and 37.5% of total HCV positive donors over a period of 3 yrs followed up with the organization(Table 4).The reasons for low rate of follow up could be due to lack of knowledge about the disease and some of them were daily wagers and did not want to miss their daily earnings during their follow up.Some donors stayed at far off places and preferred to take treatment from their family physicians and some others could not be contacted due to change of address or contact number.These problems could be overcome by recruiting more medical personnel and dedicated social workers to pursue these donors for follow up.

In this study the common history given by the donors was past history of jaundice.In our country promiscuous sexual activity is considered as a social taboo,so donors tend to conceal this history.The donors referred to the NGO were followed up with viral assays,liver function tests and other blood investigations as required and advised by a gastroenterologist working at the NGO.This included constant monitoring of donors in terms of alanine aminotransferase (ALT) levels and HBV DNA levels.Five donors had their family members screened at the NGO and all were negative for Hepatitis B and C virus.They were vaccinated later.

Active chronic HBV can be differentiated from inactive carrier state by an arbitrary serum HBV DNA level of more than or equal to 1,00,000 copies /ml as proposed by United States National Institute of Health(NIH).[17] Two clinical forms of HBeAg negative chronic Hepatits B exist.The first one is the inactive carrier state with complete absence of HBeAg ,lack of symptoms ,persistently elevated ALT and low or undetectable HBV DNA(<1,00,000 copies /ml).Ijaj et al carried out a revised cutoff values of ALTand HBV DNA levels to differentiate HBeAg negative chronic inactive from active carriers.[18] In this study 8 donors who followed up at the NGO were HBeAg positive(Pie chart 1) and thus they were HbeAg positive chronic hepatitis B donors.65 of the total 68 donors who were HBeAg negative had HBV DNA levels less than 1,00,000 copies /ml.According to the literature these donors were in the "inactive carrier state". Only 3(3.95%) of the 68 HBeAg negative donors had HBV DNA levels >1,00,000/ml with serum ALT levels more than twice the normal in our study.These can be referred as "HBeAg negative chronic hepatitis B."[18]A recent study by Kim et al(2011) validates the performance of ALT and HBV DNA and found that these markers may also be used to distinguish patients with HBeAg negative active carriers from inactive.These findings suggest that HBV DNA load and ALT are most convenient techniques to predict chronic HBV in HBeAg negative patients.[20]One of the 8 HBeAg positive donors in our study received injection alpha interferon as he had persistently elevated HBV DNA and raised ALT levels over a period of follow up of 42 weeks.His HBeAg status became nonreactive and HBV DNA levels came down to undetectable levels and is currently not under any treatment.

Of the 10 HCV positive donors ,4 of them underwent HCV genotyping.Genotype 3 was found in 3 cases and 1 case was positive for genotype 1.Chakravarty et al (2011)studied the distribution pattern of HCV genotype and its association with viral load.According to them genotypes 1,2 and 3 are widely distributed throughout the world.Genotype 2 is less common than genotype 1 and is present in most developed countries .In India genotype 3 is predominantly seen in north India and in the south there is high occurrence of genotype 1 followed by 3.[21]The authors stated that the viral load seems to be a a valuable predictive marker for the outcome of antiviral therapy as ALT levels don't reflect the disease activity and patients with high viral load respond poorly to interferon therapy.

We observed in our study that regular follow up of Hepatitis B and C positive blood donors with viral assays and liver function tests helps to distinguish between chronic inactive carriers and those suffering from chronic hepatitis. Also screening of the family members and their vaccination helped to reduce the spread of the disease.

Conclusion:

Safe blood is a critical component in improving health care,the importance of quality and safety of blood transfusion cannot be understated.We recommend more such studies to be carried out on a large scale for the benefit of voluntary blood donors who otherwise remain undetected and miss the opportunity of diagnosis and treatment.We recommend more such NGOs to come forward and undertake such projects on a large scale and Government should implement different schemes and support these NGOs to carry out such programmes on a national level.This will definitely reduce the burden of the disease in the community and ensure safe blood to those requiring transfusion.

Table 1.Yearwise total blood collection during the study period.

Year	Total blood collection
August 2009-July 2010	14,285
August 2010-July 2011	17,203
August 2011-August 2012	15,781
Total	**47,269**

Table 2:Correlation of yearwise blood collection with total number of HBsAg and HCV positive donors

Year	Total collection	Total HBV positive	Percentage (%)	Total HCV positive	Percentage(%)
August 2009-July2010	14,285	178	1.25	26	0.18
August 2010-July 2011	17,203	193	1.12	35	0.20
August 2011-August 2012	15,781	181	1.15	35	0.22
Total	**47,269**	**552**	**1.17**	**96**	**0.20**

Table 3:Comparison of Hepatitis B and Hepatitis C positivity in voluntary and replacement blood donors.

Year	Voluntary donors	HBV positive donors	HCV positive donors	Replacement donors	HBV positive donors	HCV positive donors	Total collection	HBV positive donors	HBV positive donors	Total collection
Aug 09-July 10	11,883 (83.19%)	144 (1.21%)	15 (0.13%)	2,402 (16.81%)	34 (1.42%)	11 (0.46%)	14.285	34 (1.42%)	34(1.42%)	14,285
Aug 10-July 11	14,233 (82.74%)	153 (1.07%)	30 (0.21%)	2,970 (17.26%)	40 (1.35%)	5 (0.17%)	17,203	40 (1.35%)	40(1.35%)	17,203
Aug 11-Aug 12	13,312 (84.35%)	136 (1.02%)	29 (0.22%)	2,469 (15.65%)	45 (1.82%)	6 (0.24%)	15,781	45 (1.82%)	45(1.82%)	15,781
Total	39,428 (83.41%)	433 (1.10%)	74 (0.19%)	7,841 (16.59%)	119 (1.52%)	22 (0.28%)	47,269	119 (1.52%)	119(1.52%)	47,269

Table 4:Yearwise followup of Hepatitis B positive and Hepatitis C positive blood donors with the NGO.

Year	Total HBV positive	HBV at NGO	Percentage(%)	Total HCV positive	HCV at NGO	Percentage (%)
Aug 09-July 10	178	19	10.67	26	11	42.31
Aug 10-July 11	193	22	11.40	35	9	25.71
Aug 11-Aug 12	181	35	19.34	35	16	45.71
Total	**552**	**76**	**13.77**	**96**	**36**	**37.50**

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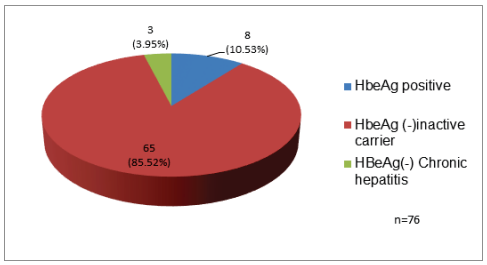

Fig 5: Pie diagram showing HBeAg status among HBsAg positive blood donors

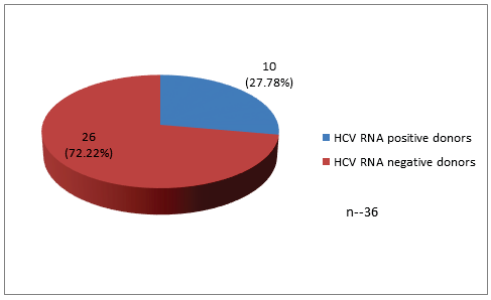

Fig 6: Pie diagram showing distribution of HCV positive blood donors according to HCV RNA status

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