Prevalence of hepatitis B and C in thalassemic children in Punjab

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Summary

Objective. Thalassemic children are dependent on regular blood transfusions in order to sustain health and life. Thus, they are significantly exposed to transfusion transmitted diseases. This study was conducted to estimate the prevalence of hepatitis B and C in a group of multitransfused thalassemic children in Punjab.

Methods. 116 children, ages seven and a half months to eighteen years, were studied for one year (1st February 2003 to 31st January 2004). They were screened for the presence of viral markers by a third generation ELISA test. Results were confirmed by polymerase chain reaction for nuclear material.

Results. The prevalence of anti-HCV was found to be 59.4% while that of HBsAg was 0.8%. HCV RNA was positive in 58.9% of the 56 seropositive patients tested. HBV DNA was not found in the solitary HBsAg positive case.

Conclusion. Despite modern day screening practices for transfusion transmitted diseases used by most blood banks, multitransfused thalassemic patients remain at risk for acquiring hepatitis virus especially hepatitis C, as was found in 59.4% of our patients. Hepatitis B, fortunately, is on the decline because of the extensive use of an effective vaccine and better developed donor screening. This emphasizes the need for universal blood screening and methods more efficient at detecting hepatitis C.

Key words: thalassemia, hepatitis B, hepatitis C.
Introduction

Thalassemia patients are at a high risk of transfusion transmitted diseases. Post transfusion hepatitis B and C present a major problem in India because of low viraemia and mutant strain undetectable by routine ELISA (1). The advent of new screening techniques and the development of an effective vaccine have substantially reduced the incidence of infection with Hepatitis B virus.

The hepatitis C virus is now known to be the most common cause of hepatitis after blood transfusion (2). Despite the vast burden of thalassemia in India there are many centers that do not follow adequate screening guidelines prior to blood transfusion. This results in a continuing risk of transmission of infectious agents in children receiving multiple blood transfusions. There is a paucity of literature emphasizing the magnitude of transfusion associated viral hepatitis in thalassemics in Punjab. Therefore this study was aimed at the determination of the prevalence of hepatitis B and C in thalassemic children in this region.

Methods

The study group consisted of the 116 children who were registered and managed in the Thalassemia Section of the Department of Pediatrics, Dayanand Medical College and Hospital, Ludhiana, over the period of one year from 1st February 2003 to 31st January 2004. Only patients who had been confirmed as thalassemics clinically and with relevant investigations were accepted as subjects. In all thalassemic children who had received more than 20 blood transfusions quantitative measurement of ferritin in serum was done. The patients were screened initially for the presence of viral markers. A qualitative third generation enzyme-linked immunosorbent assay, Ortho Antibody to HBsAg ELISA Test System 3, was used for the detection of hepatitis B surface antigen (HBsAg) in serum. A qualitative, enzyme-linked immunosorbent assay, Ortho HCV 3.0 ELISA Test System with enhanced SAVe, was used for the detection of antibody to hepatitis C virus (anti-HCV) in serum.

In seropositive children, qualitative detection of hepatitis C virus RNA and hepatitis B virus DNA was done by polymerase chain reaction (PCR).

Statistical analysis

The data were subjected to statistical analysis using SPSS version 10.0 software. Mean and standard deviations were computed. For discrete variables, Chi square test was applied to determine the association between two variables. Students’ t test was done to compare the mean of two groups. Significant difference was accepted at p = .05.

Observations

The thalassemic children were aged between seven and a half months to eighteen years. The mean age of the children was 7.39 ± 4.8 years, with 43.9% in the age group of 0-5 years. The age of diagnosis ranged between two and a half months to nine years with a mean of 1.33 ± 1.6 years.

The mean annual hemoglobin was 9.03 ± 0.95 g/dl with a range of 5.6 to 11 g/dl. In our study 69.8% of the children were males. Male to female ratio was 2.3:1.

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>Total patients</th>
<th>Anti-HCV positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5.0</td>
<td>51</td>
<td>17</td>
</tr>
<tr>
<td>5.1-10.0</td>
<td>34</td>
<td>29</td>
</tr>
<tr>
<td>&gt; 10.0</td>
<td>31</td>
<td>23</td>
</tr>
<tr>
<td>Total</td>
<td>116</td>
<td>69</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of transfusions</th>
<th>Total patients</th>
<th>Anti-HCV positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 or fewer</td>
<td>22</td>
<td>1</td>
</tr>
<tr>
<td>21-50</td>
<td>31</td>
<td>15</td>
</tr>
<tr>
<td>51-100</td>
<td>22</td>
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<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>116</td>
<td>69</td>
</tr>
</tbody>
</table>
A large number (77.5%) of the children had received blood transfusions from private nursing homes. Most children had received transfusions from multiple hospitals. The mean number of blood transfusions received by the children was 82.4. The mean annual serum ferritin level in the children was 3842.5 ng/ml (±1863). Of the 22 children who had received fewer than 20 transfusions, serum ferritin was not done in 21, and in one patient ferritin levels had been measured outside our institution.

Anti-HCV was positive in 69 children, resulting in a prevalence of 59.4%. HbsAg was positive in only 1 patient (prevalence = 0.8%). HCV RNA was drawn in 56 patients, of whom 33 (58.93%) tested positive. HBV DNA was sent in 1 child and was negative.

In our study, as the age increased, the percentage of children who were anti-HCV positive children increased and these findings were statistically significant. (p value < 0.05) (Table 1). As expected, the prevalence of seropositivity also increased significantly with the number of transfusions (p value < 0.01) (Table 2). All children who had received more than 200 transfusions (4 cases) were found to be anti-HCV positive.

Since it relates to the number of transfusions, the rise in serum ferritin levels also directly related to a rise in anti-HCV seropositivity (p value < 0.01) (Table 3). In children having serum ferritin greater than 3000 ng/ml, the seropositivity was higher than 70%, and 100% seropositivity was seen in those children who had serum ferritin higher than 7000 ng/ml.

In a comparison of hepatitis C seropositive children to seronegative children, ferritin levels were significantly higher in the seropositive children as was the number of transfusions received by them (Table 4).

### Discussion

Post transfusion hepatitis is a leading cause of morbidity in thalassemic children. Studies conducted in various parts of India in multitransfused patients show a prevalence of HBsAg ranging between 5.7% and 45% (3-6) and the prevalence worldwide is reported to be between 0 to over 13% (7-11). In the present study only one patient tested positive for HBsAg accounting for a prevalence of 0.8%. Most children in the study group (93.1%) had received vaccination against hepatitis B (three doses). This is much higher than what was reported in 1992 by Williams et al. in Delhi (14.8%) (12). The decrease in prevalence of hepatitis B in our study could be explained by the routine practice of vaccination in all thalassemic children as well as the use of the sensitive ELISA test to screen all blood donors against hepatitis B in our blood bank starting in 1985.

In our study anti-HCV was positive in 69 of the 116 patients, yielding a prevalence of 59.48%. This prevalence is higher than that reported in the studies in other parts of India (11.1 to 30%) (3-5, 12).
The increased prevalence of hepatitis C found by this study could be attributed to the fact that the children registered with us had been receiving blood transfusions from multiple hospitals. A large percentage (77.5%) had received blood transfusion from private nursing homes where strict blood screening is not followed. Only eleven of the 69 anti-HCV positive patients had received blood solely from teaching hospitals, and just three of them had been transfused exclusively at DMCH. These three children were aged 2 years, 7 years and 8 years. Screening for hepatitis C virus was started in our blood bank in 1995. A very sensitive third generation ELISA test was used in our study for the diagnosis of hepatitis C infection and ours was a larger cohort than that in previous studies. When compared with the studies done elsewhere in the world, the prevalence of anti-HCV in our study was similar to that reported by Angelucci et al. (13), Bhatti et al. (14) and Ansar et al. (15), but higher than that reported by other researchers (7-11).

Hepatitis C virus RNA was studied in 56 of the 69 seropositive children. It was detected in 33, i.e. 58.93% of those tested, which represent the true seropositive children. The rate of RNA positive testing was higher than that reported by Irshad et al. (40%) (5).

When seropositivity was related to age, we found that increasing age significantly raised the chances of seropositivity. The likely explanation for this is the increase in the number of blood transfusions received over the years. This finding was also reported by Williams et al [12] and Ni et al (16). As expected there was a highly significant correlation between seropositivity and the increasing numbers of blood transfusions received. This has also been recognized by Ansar et al (15) and Singh et al (6). Increasing serum ferritin levels, which also correlate with increased transfusions, were also associated with a significant rise in seropositivity. Similar results were seen in the studies conducted by Prati et al (17) and Li et al (9).

It is evident that post transfusion hepatitis is a major complication in thalassemic children who have multiple donor exposures. Given the prevalence of hepatitis B and C viruses in the donor population and the inadequacy of screening practices, this problem is still considerable. Screening by the third generation ELISA tests for HBsAg and anti-HCV has been started but is not routinely practiced in all blood banks. Between November 1995 and November 1996, Kapoor et al (18) conducted a nation wide questionnaire based study to assess the functioning of blood banks in India. The results revealed about 87% of the respondent blood banks screened for hepatitis B, 95% for HIV and only 6% for hepatitis C. According to the WHO survey (2004) of 178 countries, it was found that 20 countries do not have 100% screening for HIV, 24 do not regularly test for Hepatitis B and 37 ignore hepatitis C (19). Thus, strict blood transfusion safety guidelines need to be established.

Even with ELISA based blood donor screening, a residual risk of transfusion – transmitted viral infections exists. Limitations in the screening tests including false negative results, and the problems associated with the “window period” need to be addressed. This is where sensitive nucleic acid tests have a role. Though not 100% effective, nucleic acid amplification tests (NAT) narrow the infectious window and exponentially reduce the viral load detectable by serological screening (20).

References


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