Thalassemia and other Hemoglobinopathies in Bangladeshi Children

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Abstract: Background- Worldwide, Thalassemia and Hemoglobinopathies are the most common inherited disorders with a wide geographical variation in incidence. Bangladesh is situated in a thalassemia tending region but this hereditary disorder receives little attention yet and unfortunately there is no definitive national data regarding incidence and socio-demographic profile of Thalassemia and Hemoglobinopathies in the country. Objective- This study was undertaken to determine the current situation of the occurrence and socio-demographic profile of thalassemia and other hemoglobinopathies among Bangladeshi children. Methods- It was a prospective study conducted from January 2015 to December 2016. All newly diagnosed children with Thalassemia major and other Hemoglobinopathies in Dhaka Shishu Hospital (children) Thalassemia center were included in the study. Consideration was given to total number of cases, age at presentation, sex distribution and types. Hb% was done in every patient after enrollment. Result- Among total 432 affected children, male female ratio was 1.6:1 in which E-β Thalassemia, β Thalassemia major and Hb E disease were 68.50%, 31% and 0.5% respectively. Consanguineous marriage was found in 14% parents. Conclusions- E-β Thalassemia was found the commonest type of thalassemia among Bangladeshi children.

Keywords: Thalassemia, Hemoglobinopathies, Children

1. Introduction

The hereditary disorders of hemoglobin are the most common single gene disorder with a wide geographical variation in incidence, widely in a broad belt ranging from Mediterranean area (Cyprus, Sardinia, several regions of Continental Italy) and parts of North and West Africa through the Middle East, Bangladesh, India, Sri Lanka, Thailand and other countries of South East Asia [1-2]. The hereditary disorders of hemoglobin are classified broadly into groups: The Thalassemia and haemoglobinopathies[3]. Thalassemia is characterized by reduction or absent production of one or more of the globin chain that make up the hemoglobin (Hb) tetramers, which is the commonest autosomal recessive disorder worldwide [4]. In general, thalassemia can be classified into two pivotal forms: α-thalassemia and β-Thalassemia. α-thalassemia is characterized by impaired synthesis of α globin chain and β-Thalassemia, the most common type of thalassemia, is due to impaired β globin chain synthesis[5]. The hemoglobinopathies are characterized by the production of structurally defective hemoglobin due to abnormalities in the formation of the globin moiety of the molecule [3]. Among more than 300 structural variants, Hb E is the second most prevalent hemoglobin disorder in the world characterized by mutation in beta-globin gene causing substitution of glutamic acid for lysine at position 26 in beta-globin chain [2]. Hb E presents in 3 forms namely heterozygous state (Hb E Trait), homozygous state (Hb E disease) and compound heterozygous states as Hb Eβ Thalassemia, Sickle Cell- Hb E disease [6], Hb Eβ Thalassemia is quite common condition which is becoming an important health issue in Thailand, a large part of Southeast Asia extending from Indonesia to Sri Lanka and Northeast India [7-8]. These inherited disorders of hemoglobin are characterized by chronic hemolytic anemia, typically requires life-long blood transfusion (BT) therapy for patients survival [9]. Pathophysiology is complex which involves ineffective erythropoiesis, apoptosis, Oxidative damage and shortened red cell survival [8]. Regular blood transfusion prevents many complications in thalassemic patient which are introduced by ineffective erythropoiesis but on the other hand, can produce morbidity and mortality due to toxic iron accumulation in heart, endocrine glands and other organ [10]. Thus a thalassemic child and the family undergoes through a socio-economic strain and ultimately causes the burden for the whole community[11]. Bangladesh, a developing country having population of over 160 million, situated in a thalassemia prone region [12]. But, there is no national data regarding the number, distribution or socio-demography of thalassemia patient in the population.
country. Khan et al estimated that existing thalassemia patient in Bangladesh is about 1 lac and suspected total number of β-thalassemia major and Hb Eβ-thalassemia born around 1040 and 6443 per year respectively in the country [13]. There is also lack of definitive data regarding existing thalassemia carrier in Bangladesh. A conservative WHO report has shown that 3% of population carries β-thalassaemia and 4% carries Hb-E in Bangladesh [14]. The rapidly growing number of children diagnosed as thalassaemia in Bangladesh clearly indicate that thalassemia will be an emerging health burden for our country. As, Thalassaemia is a hereditary disease, it is only manageable when it is prevented. And for planning of a successful prevention program, first of all, we should know the regional accurate data of population frequency on status and distribution of thalassemia and other hemoglobinopathies in Bangladesh. The aim of the study is to observe the current situation of the occurrence and socio-demographic profile of thalassemia and other hemoglobinopathies among children in Bangladesh.

2. Methods

It was a prospective study carried out for a period of two years from January 2015 to December 2016 in Dhaka Shishu Hospital (children) Thalassemia center, the largest referral thalassaemia center for children in Bangladesh. All newly diagnosed children with Thalassemia and other Hemoglobinopathies during this study period were included in the study. After enrolment, all the data related to demographic profiles (name, age, sex), total number of cases, age at presentation, sex distribution and types were noted in a preformed datasheet on a structured proforma and the data entered and analyzed for frequency, percentages and means on SPSS version 19. Hb% was done in every patient after enrollment.

4. Results

During the study period, total 432 newly diagnosed children with thalassemia major or other Hemoglobinopathies were enrolled in the study when diagnosis was confirmed by Hb-electrophoresis. Among them, we found Hb Eβ-thalassemia in total 296 (68.50%) children, β Thalassemia major was in 31% (134 children) cases and Hb E disease was found in only 2 (0.5%) children. We did not find any α-thalassemia during this study period. (Figure 1) Among total affected children, male were 270 (62%) and female were 162 (38%) with a male female ratio of 1.6:1. This male predominant picture was also found in individual type of Thalassemia shown in Figure 2. Out of total 296 children having Hb Eβ-Thalassemia 65.20% (193 children) was male and 34.80% (103 children) was female. In case of β Thalassemia major and Hb E disease, male was in 56% and 50% cases respectively.

![Figure 2: Individual sex distribution among different types of Thalassemias in children](image)

The age at the diagnosis of children having thalassemia major or other Hemoglobinopathies are shown in Table 1.

Table-1: Age at diagnosis of Thalassemia in children in DSH (n=432)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No of children</th>
<th>Age range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt; 2yr</td>
</tr>
<tr>
<td>Eβ-Thalassemia</td>
<td>296</td>
<td>32(10.8%)</td>
</tr>
<tr>
<td>β Thalassemia major</td>
<td>134</td>
<td>68(51.34%)</td>
</tr>
<tr>
<td>Hb E disease</td>
<td>2</td>
<td>1(50%)</td>
</tr>
</tbody>
</table>

Our observation, 51% β Thalassemia major children was diagnosed at less than 2 year of age whereas majority E-β Thalassemia was diagnosed at more than 2 years of age (Fifty five percent at 2-4 year and 34.12% at above 4 year of age) and only 10.8% children having E-β Thalassemia was diagnosed at below 2 year of age. We found, only two HbE disease in the series. One of them was diagnosed at 1 year and other was at 3 year 4 month of age. Consanguineous marriage was found among total 61 (14%) parents of affected children.
Hb% at the time of diagnosis of children having thalassemia major or other Hemoglobinopathies are shown in Table II.

In the current study, we observed that, at the time of diagnosis, 52.98% of children who had β Thalassemia major was severely anemic, whereas in HbE-β Thalassemia, 81.75% children was moderately pale (Table III).

Table II: Hb% at the diagnosis of Thalassemia in children in DSH (n=432)

<table>
<thead>
<tr>
<th>Types of Thalassemia and other Hemoglobinopathies</th>
<th>Hb% (mg/dl) at the diagnosis</th>
<th>Range</th>
<th>Median</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-β Thalassemia</td>
<td>3.8-11.4</td>
<td>7.6</td>
<td>6.1±</td>
<td>0.485</td>
</tr>
<tr>
<td>β Thalassemia major</td>
<td>2.2-11.0</td>
<td>6.6</td>
<td>4.9±</td>
<td>1.016</td>
</tr>
<tr>
<td>Hb E disease</td>
<td>4.5-6.8</td>
<td>5.7</td>
<td>5.6±</td>
<td>1.151</td>
</tr>
</tbody>
</table>

Table III: Distribution of children by severity (according to WHO15) of anemia (n=432)

<table>
<thead>
<tr>
<th>Types of Thalassemia and other Hemoglobinopathies</th>
<th>Number of children (% of total having anemia at the diagnosis)</th>
<th>Mild (10-10.9 mg/dl)</th>
<th>Moderately (7-&lt;9.9 mg/dl)</th>
<th>Severe (&lt;7 mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbE-β Thalassemia</td>
<td>9 (3.04%)</td>
<td>242 (81.75%)</td>
<td>45 (11.82%)</td>
<td></td>
</tr>
<tr>
<td>β Thalassemia major</td>
<td>11 (8.20%)</td>
<td>52 (38.80%)</td>
<td>71 (52.98%)</td>
<td></td>
</tr>
<tr>
<td>Hb E disease</td>
<td>00</td>
<td>01 (50%)</td>
<td>01 (50%)</td>
<td></td>
</tr>
</tbody>
</table>

5. Discussion

Bangladesh is situated in a thalassemia tending region [12] but, at national level, there is no population based data or thalassemia registry in the country. In this present study, we attempted to observe the current situation of the occurrence and socio-demographic profile of thalassemia and other hemoglobinopathies among children in our set-up. However, it does not give a true prevalence in the total population. But Dhaka Shishu (Children) Hospital thalassemia Center is the largest, comprehensive, referral thalassemia Center for children in Bangladesh. As, these children were referred from different districts of the country, hence, hospital based data such as ours is an important sources of epidemiologic information for education, planning for prevention and further research about thalassemia and other hemoglobinopathies in Bangladesh.

In the series we found that HbE-β Thalassemia was the commonest (68.5%) among all types of hereditary hemoglobin disorders. Mannan et al. (2013) reported the similar finding in their study conducted in two different hospitals in Chittagong town in Bangladesh and they found that HbE-β Thalassemia was the most common among all types of hemoglobin formation disorders amounting 38.65% of total 207 patients [16]. In other study in Bangladesh Palit et al. (2012) found that HbE-β Thalassemia was 77.4% among the total 53 patients having thalassemia syndrome [17]. Fucharoen et al. (2000) and George et al. (1993) also reported that HbE-β Thalassemia is the commonest form of thalassemia in southeast Asia [18-19]. Actually, approximately 50% affected patient with severe thalassemia are suffering from HbE-β Thalassemia [20-21]. In the current study, we found Hb E disease in only 2 (0.5%) children but Hasan et al. (2013) and Uddin et al. (2010) found Hb E disease in Bangladesh in 30% and 5.71% cases respectively [22-23]. This may be due to the age of the study population. We conducted the study only in pediatric age group. We did not find any α Thalassemia, sickle cell disease or Hb D variant. Sickle cell disease is the most common in people of African ancestry and tribal people of India [24]. On the other hand Hb D occurs in Iran, Pakistan and northwest part of India [3].

Our data showed that the occurrence of thalassemia syndrome was more common in male child. Similar data was found in other studies in Bangladesh conducted by Mannan et al. (2013), Palit et al. (2012) and Aziz et al. [16-17,20]. The M/F ratio observed in our series was also consistent with the values reported in India [20-21]. This picture might be due to either thalassemia is more common in male in this region nor the gender biasness among the parents who spend more attention to the illness of their male children.

In this series, our observation, 51% β Thalassemia major children was diagnosed at less than 2 year of their age whereas majority of E-β Thalassemia was diagnosed at more than 2 years of age (Fifty one percent at 2-4 year and 34.12% at above 4 year of age) and only 10.8% children having E-β Thalassemia was diagnosed at below 2 year of age. Mannan et al. (2013) found that the incidence was high in the age group between <1-10 year in all types of Thalassemia and hemoglobinopathies [16]. In the current study, we observed that, at the time of diagnosis, 52.98% of children who had β Thalassemia major was severely anemic, whereas in HbE-β Thalassemia, 81.75% children was moderately pale. The findings observed by Aziz et al. (2009) in case of HbE-β Thalassemia was consistent with the present study [20]. Findings are
also similar to the findings in United Kingdom [25].
In Bangladesh, the most of the people is Muslim and due to sociocultural practices, marriage among cousins is common in the country. As, Thalassemia is an autosomal recessive disorder, consanguineous marriage is an important factor regarding occurrence and preventive issue of Thalassemia and hemoglobinopathies. But the accurate data regarding consanguninity is not known in Bangladesh. In this study, we found consanguineous marriage among 14% parents of affected children.
This study has certain limitations. We did not include Thalassemia Minor or other carrier state of Hemoglobinopathies in the current study and finally it is a single center study. Further a large, multicenter and population-based study is needed in order to accurate micro-mapping the current situation of the occurrence, frequency and socio-demographic profile of thalassemia and other hemoglobinopathies among children in Bangladesh.

6. Conclusions

HbE-β Thalassemia was found the commonest type of thalassemia among Bangladeshi children. Consanguineous marriage was found in 14% parents of affected child. For education, further planning of a successful prevention program of thalassemia and other hemoglobinopathies in Bangladesh, this study might be an important pave.

7. References


