**ORIGINAL ARTICLE**

**Incidence, characteristics and laboratory parameters of epistaxis in children with β-Thalassemia major at a Tertiary Care Hospital of South Punjab, Pakistan.**

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**ABSTRACT... Objective:** To find out the incidence, characteristics and laboratory parameters of epistaxis in children with β-thalassemia major visiting a tertiary healthcare facility of South Punjab, Pakistan. **Study Design:** Retrospective study. **Setting:** Department of Hematological Diseases, Thalassemia and Bone Marrow Transplantation Centre, and Department of Biochemistry, Bahawal Victoria Hospital, Quaid e Azam Medical College, Bahawalpur, Pakistan. **Period:** January 2021 to November 2022. **Material & Methods:** The hospital record of children of both genders aged from 2 to 18 years of age with blood transfusion dependent β-thalassemia was analyzed. Children reporting at least 1 episode of epistaxis in the preceding period were included in the final analysis to find out the incidence, characteristics and laboratory findings of children presenting with of epistaxis. **Results:** Out of 3772 children with β-thalassemia major, 85 reported at least 1 episode of epistaxis showing the incidence of epistaxis as 22.5/1,000 cases of β-thalassemia major. The mean age of the children at the time of enrollment and at the time of diagnosis of thalassemia was 9.93±3.48 years and 1.23±1.26 years respectively. The mean monthly frequency of blood transfusion was 1.71±0.75 blood transfusions per month. The mean monthly epistaxis frequency was reported to be 2.35±1.71 while 59 (69.4%) children had 2 or more than 2 monthly episodes of epistaxis. The mean serum ferritin level was noted to be 4058±2173 ng/ml. Ultrasonography findings revealed mean spleen size to be 9.25±5.80 cm. **Conclusion:** The incidence of epistaxis episodes among children with β-thalassemia was very high. Chronic iron-overload seemed to be common abnormality among children with β-thalassemia that should be addressed to potentially reduce the risk of epistaxis among these children.

**Key words:** β-thalassemia, Epistaxis, Hemoglobin, Serum Ferritin, Spleen.

**INTRODUCTION**

Thalassemia is known to be the commonest single gene abnormality globally.¹ Thalassemia consists of a group of hemolytic abnormalities and it is thought that around 1.5% of the global population are β-thalassemia carriers.² It is further estimated that there is an addition of 50000 to 60000 newborns globally who have thalassemia.³ Mediterranean, Middle-East, South East Asian and African regions are the most affected parts of the world with thalassemia.⁴ Pakistan is amongst the countries where the burden of thalassemia is on the higher side while estimates have calculated that between 8-10 million of the local population are carriers of thalassemia. Epidemiological records have shown that there is an increase of 5,000 to 9,000 thalassemia cases every year locally.⁵,⁶

Epistaxis is described as “acute haemorrhage from the nostril, nasal cavity or nasopharynx”.⁷ Epistaxis is considered to be a frequent presentation among children and data has shown that more than 50% of the children below 15 years of age report at least one experience of epistaxis.⁸,⁹ The severity of epistaxis can be ranging between a single less concerning episode to a much severe and life-threatening episode that may need urgent medical attention or intervention.¹⁰ The origin of bleeding is through venous plexus or kiesselebach among most of the

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children presenting with epistaxis while epistaxis is self-limiting among a vast majority of the cases. Some past researches have attributed the recurrence of epistaxis to hypersplenism and/or thrombocytopenia while some others have described it to be due to thromboinflammatory mechanisms.

To the best of our knowledge, no real data exists regarding the incidence of epistaxis among children with β-thalassemia in the international or national literature so the present study was designed to reveal the burden of epistaxis among children registered in the local registry of one of the leading tertiary care hospital of South Punjab, Pakistan. The findings of this study were thought to help us provide epidemiological data about the proportion epistaxis affecting children who are visiting the healthcare facility for regular follow ups and blood transfusions. The objective of this research was to find out the incidence, characteristics and laboratory parameters of epistaxis in children with β-thalassemia major visiting a tertiary healthcare facility of South Punjab, Pakistan.

MATERIAL & METHODS
This retrospective study was done at “The Department of Hematological Disorder, Thalassemia and Bone Marrow Transplantation Centre, and Department of Biochemistry, Bahawal Victoria Hospital, Quaid e Azam Medical College”, Bahawalpur, Pakistan during January 2021 to November 2022. Approval from “Institution’s Ethics Committee” was acquired (letter number: 2041/DME/QAMC Bahawalpur). Informed as well as written consents were taken from parents/guardians of all study participants. The hospital record of children of both genders aged from 2 to 18 years of age with blood transfusion dependent β-thalassemia was analyzed. All children included in this study were being administered regular monthly blood transfusions for keeping the haemoglobin levels between 9-10 g/dl. Children reporting at least 1 episode of epistaxis in the preceding period were included in the final analysis to find out the incidence of epistaxis and their characteristics. Children having comorbid hemoglobinopathies were not included in this research.

In children with epistaxis, demographic information of children including age, gender, age at the time of diagnosis of thalassemia, residential status, bleeding site, frequency of epistaxis, monthly frequency of blood transfusion and spleen size were noted. Important laboratory parameters like platelet count, hemoglobin level, prothrombin time (PT) and activated partial thromboplastin clotting Time (APTT) were also taken into evaluation. Platelet count between 150-400 (x10⁹/L) was considered normal. The reference range for PT and APTT were considered as 60-70 seconds and 30-40 seconds respectively. Total serum bilirubin count between 0.1-1.2 mg/dl was taken as normal. Serum ferritin levels between 7-140 ng/ml was considered as normal. Ultrasonography findings were also noted including spleen size. A special format was made to record all study information.

Study data was entered and analyzed employing “Statistical Package for Social Sciences (SPSS)” version 26.0. Descriptive statistics were employed for data representation. The incidence of epistaxis per 1,000 children with β-thalassemia was calculated. Furthermore, categorical variables were represented as frequencies and percentages. Numerical variables were described as mean and standard deviation (SD).

RESULTS
During the study period, a total of 3772 children as per inclusion and exclusion criteria visited the study center. Out of these 3772 children, 85 reported at least 1 episode of epistaxis in the preceding period and were included in the final analysis. The incidence of epistaxis was calculated to be 22.5/1,000 cases of blood transfusion dependent thalassemia.

In a total of 85 children with epistaxis episodes, 51 (60.0%) were boys while 34 (40.0%) were girls representing a boys to girls ratio of 1.5:1. The mean age of the children at the time of enrollment and at the time of diagnosis of thalassemia was 9.93±3.48 years and 1.23±1.26 years respectively. Residential status of 66 (56.5%)
children was rural. Parental consanguineous marriage was noted among 63 (74.1%) cases. The mean monthly frequency of blood transfusion was 1.71±0.75 blood transfusions per month. Most common site of bleeding was both nostrils, reported in 46 (54.1%) children. Table-I is showing characteristics of children studied with epistaxis episodes.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>51 (60.0%)</td>
</tr>
<tr>
<td>Girls</td>
<td>34 (40.0%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>2-5</td>
<td>10 (11.8%)</td>
</tr>
<tr>
<td>6-10</td>
<td>36 (42.4%)</td>
</tr>
<tr>
<td>11-18</td>
<td>39 (45.9%)</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>19 (43.5%)</td>
</tr>
<tr>
<td>Rural</td>
<td>66 (56.5%)</td>
</tr>
<tr>
<td>Age at the time of diagnosis of thalassemia (years)</td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>47 (55.3%)</td>
</tr>
<tr>
<td>≥1</td>
<td>38 (44.7%)</td>
</tr>
<tr>
<td>Parental Consanguineous Marriage</td>
<td>63 (74.1%)</td>
</tr>
<tr>
<td>Frequency of Blood Transfusion per Month</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>38 (44.7%)</td>
</tr>
<tr>
<td>2</td>
<td>36 (42.4%)</td>
</tr>
<tr>
<td>3</td>
<td>9 (10.6%)</td>
</tr>
<tr>
<td>4</td>
<td>2 (2.4%)</td>
</tr>
<tr>
<td>Bleeding site</td>
<td></td>
</tr>
<tr>
<td>Right Nostril</td>
<td>10 (11.8%)</td>
</tr>
<tr>
<td>Left Nostril</td>
<td>8 (9.4%)</td>
</tr>
<tr>
<td>Both Nostrils</td>
<td>46 (54.1%)</td>
</tr>
<tr>
<td>Both Nostrils + Teeth/Gums</td>
<td>14 (16.5%)</td>
</tr>
<tr>
<td>One Nostril + Teeth/Gums</td>
<td>7 (8.2%)</td>
</tr>
</tbody>
</table>

The mean monthly epistaxis frequency was reported to be 2.35±1.71 while 59 (69.4%) children had 2 or more than 2 monthly episodes of epistaxis. Figure-1 is showing the frequency of epistaxis episodes per month among children.

Ultrasonography findings revealed mean spleen size to be 9.25±5.80 cm. Table-II is showing descriptive statistics about the clinical characteristics of children with epistaxis.

DISCUSSION
The burden of epistaxis among children on blood transfusion dependent thalassemia is not well documented. This study is amongst the first that revealed that incidence of children with epistaxis episodes among β-thalassemia children to be 22.5/1,000 children which seems very high. The presence of epistaxis has been documented
in children with β-thalassemia. Epistaxis episodes among these children could be lined with hepatic dysfunction due to iron overload that could further be attributed to regular blood transfusions. Some researchers have shown that hepatic dysfunction is not clearly evident until serum ferritin level reaches beyond 2,000 ng/ml. The mean serum ferritin level among present set of patients with epistaxis episodes was 4058±2173 ng/ml which seemed higher than the described cut-off which could have contributed to regular epistaxis episodes among children with β-thalassemia.

A study done by Naithani and colleagues reported bleeding episodes among children with β-thalassemia to be 29.6%. The same study reported the mean age of these children to be 9.68±4.3 years while mean serum ferritin level was 3709±1625 ng/mL which is quite close to what we observed in this research. In a previous study from our study site reported the mean age and mean serum ferritin levels to be 9.1±4.2 years 4137±2319 ng/ml which correlates well with the present data. Some researchers have highlighted that chronic consumptive state because of chronic activation of the intrinsic coagulation pathways due to regular blood transfusion administrations which could further contribute to exaggerated thrombocytopenia among children with β-thalassemia major. The presented study also reported exaggerated values of PT and APTT among β-thalassemia children with epistaxis which could be due to hepatic parenchymal injury because of iron overload state. Chronic activation of the intrinsic coagulation with or without kallikrein system that follows intravascular hemolysis and regular blood transfusion administrations could also be the mechanisms behind higher epistaxis episodes among children with β-thalassemia.

Being a retrospective study, we were unable to record data actively that could have its own limitations. Being a single center study, our findings should further be verified in other large prospective trials. The present study again raises the need for a national registry for thalassemia children that would enable us to have valuable insights about the characteristics, patterns of presentation and management strategies among these children.

**CONCLUSION**

The incidence of epistaxis episodes among children with β-thalassemia was very high. Chronic iron-overload seemed to be common abnormality among children with β-thalassemia that should be addressed to potentially reduce the risk of epistaxis among these children.

**REFERENCES**


