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OUTCOME OF IMMUNE THROMBOCYTOPENIC PURPURA (ITP). EXPERIENCE IN A TERTIARY CARE CHILDREN HOSPITAL OF BANGLADESH

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ABSTRACT

Background: The pathogenesis of Childhood ldiopathic Thrombocytopenic Purpura(ITP), a common hematological disease involves antibody-mediated platelet destruction and reduced platelet production. Though in large number of cases it resolve spontaneously but we the pediatricians very frequently use steroid or IV Immunoglobulin due to lack of experience. **Object**: The objective of this study was to review the presenting features, natural history and remission rate of ITP cases spontaneously or to therapy. **Method**: This is a retrospective study conducted in the Department of Pediatric Haematology & Oncology of Dhaka Shishu (Children) Hospital during the period January 2018 to December 2019 and there was review and analysis of natural history and treatment response in children diagnosed with ITP age ranged of 9 months to 14 years. **Results**: Of 64 patient with ITP with a age range of 9 months to 14 years (mean age 6.1 ± 1.6 yrs) and female predominance 36 (56 %) female and 28 (44 %) male. Male female ratio was I: 1.3. Ten (15.6%) children had major hemorhage. The platelet counts were 6,000/cmm to 1.25,000/cmm (mean 19,000/cmm). Bone marrow study was done in 14 (22%) cases with no alteration in diagnosis. Regarding outcome, 25 (39%) patients had been achieved spontaneous remission and 39 (61%) needed intervention with corticosteroid. Among the patients treated with corticosteroid 26 (67%) patients responded to corticosteroid and 13 (33%) had gone to chronic stage. Out of 13 chronic ITP patients 6 had received Anti D Ig: of these 6 patients 100% patients maintained platelet count >30,000/cmm for variable periods, and 7 patients received oral Eltrombopag-a newer drug of ITP treatment: of these 7 patients 5(71%) had responded and maintaining platelet count >50,000/cmm for longer duration than Anti D and 2(29%) did not respond. These 13 of 64 (20%) patient remained as chronic ITP. Chronic ITP developed in older children. **Conclusion**: The overall prognosis in childhood ITP is excellent. Spontaneous remission occurred in good number of cases (39 %) and overall about 90% cases resolved with therapy or observation. Anti-D Immunoglobulin and Eltrombopag are promising in chronic ITP though further larger study is needed.

KEYWORDS: ITP, Outcome.

INTRODUCTION

Pediatric immune thrombocytopenia (ITP) is an acquired immune-mediated disorder characterized by isolated thrombocytopenia.[1,2] ITP is characterized by autoreactive antibodies that bind to platelets targeting them for phagocytosis by macrophages in spleen and liver.[3,4] Other mechanisms, includin0g B-cell hyperreactivity, T-cell mediated cytotoxicity and impaired platelet production, have also been demonstrated to cause ITP.[5-7]

ITP can be classified based on patients age (childhood versus adult)', duration of illness (acute versus chronic) and presence of an underlying disorder (primary versus secondary). Persistance of thrombocytopenia (<1,50,000 /cmm) for longer than 12 months are defined as chronic ITP.[8]

Although ITP is often self-limiting, about 20-30% of children develop chronic ITP, defined as persistence of thrombocytopenia (<150x10'L) for longer than 12 months.[9] In the chronic form, therapeutic choices are complex and focused on improving health-related quality of life[10] and controlling bleeding symptoms.[11,12]

Corticosteroids and IVIG are recommended as first-line treatments. If first-line therapy fails, therapeutic options

for managing chronic ITP include immunosuppressive drugs (such as rituximab, mycophenolate mofetil, and sirolimus).[2,13] splenectomy or, more recently, thrombopoietin receptor agonists (TPO –RAs).[14,15]

Clarification of the major pathways that lead to childhood ITP have influenced our approach to therapy and may ultimately aid in the early identification of individuals who may need more aggressive intervention versus no treatment at all. By decreasing the risk of hemorrhage and minimizing the long-term side effects of treatment, these insights have greatly improve the care of patients with ITP.[16-18] With this view this study was done to see the percentage of spontaneous recovery and to disseminate it for general pediatricians.

METHODS AND MATERIALS

This retrospective study was performed by reviewing the patient`s files / records and statistical analysis on all ITP patients admitted in the Paedxiatric Haematology & Oncology Department of Dhaka Shishu (Children) Hospital from January 2018 to December 2019. Diagnosis was done from clinical findings, peripheral blood count. Initially patients were kept in observation for spontaneous remission when initial platelet count was >10000/cmm and there was no massive haemorrhage. Platelet count was followed every day. When platelet count was <10,000/cmm or there was massive haemorthage or suspicion of ICH, intervention was done with oral corticosteroid (3-4 mg/kg/day for 7 -10 days and then tapered). Anti D Ig was given at the dose of 50 - 75 µg / kg and Eltrombopag at the dose of 25-50 mg /day. A complete response (CR) to treatment was defined as achieving a platclet count>150x10°/L and resolution of bleeding symptoms, a partial response (PR), achieving a platelet increment of >20x107L. and improvement in bleeding symptom

RESULT

Total number of patients were 64. Their age range from 9 months to 14 years (mean age 6.1±1.5 years). Their age is given in Table-1. There was female predominance, 36 (56%) female and 28 (44%) male. Male female ratio was 1: 1.3.

Table-1: Age distribution of Patients (n=64).

Age of patients	Number of Patients	Percentage
<1 Year	04	6%
1-10 Years	47	74%
<10 Years	13	20%

Bone marrow study was done in 14 (22%) patients with no alteration in diagnosis.

The platelet counts ranged from 6,000/cm to 1, 25,000/cmm (mean 19,000/cmm) (Table-2).

Table-2: Distribution of Platelet count (n=64).

Platelets Count	No of Patients	Percentage of Patients
Less than 20,000/cmm	42	64%
20,000 – 30,000/cmm	16	28%
More than 30,000/cmm	06	8%

Regarding outcome- 25 (39%) out of 64 patients went into spontaneous remission and 39(61%) needed intervention with corticosteroid (Table-3). 39(61%) needed intervention with corticosteroid (Table-3).

Table-3: Distribution of Remission Pattern (n=64).

Total Patients	Spontaneous Remission	Need Intervention
64 (100%)	25 (39%)	39 (61%)

After intervention with corticosteroid- 26 (67%) out of 39 patients responded to corticosteroid and 13 (33%) had gone into chronic stage. Out of 13 chronic ITP patients Anti-D Ig was given in 6 patients with 100% response to maintaining platelet count> 30,000/cm for variable period and 7 received oral Eltrombopag- a newer drug of ITP (Table-4). Among these 7 patients of Eltrombopag 5(71%) responded and maintaining platelet count more than 50,000/ for longer duration than Anti D group and 2(29%) did not respond.These 13 patients remained as chronic cases till now.

Table 4: Distribution of different treatment regimen & their response.

Treatment Regimen	Remission	Not in Remissionmq
Corticosteroid (39)	26 (67%)	13 (33%)
Anti D Immunoglobulin (6)	06 (100%)	Nil
Eltrombopag (7)	05 (71%)	02 (29%)

In all the responded (spontaneous & intervention) patients, platelet count began to rise at 3rd day and

continue to rise up to 7th day except in Eltrombopag group where count began to rise at 7th day & continue to rise at 25th day (Table-5).

We found that 3 (50%) patients maintaining platelet count >50,000/cmm for at least 15 weeks.

Table 5: Mean Platelet count (Thousand/ Cmm.) at treatment.

Treatment	Day 0	Day 3	Day 7	Day 15	Day 25
No treatment	17	28	85	173	230
Coticosteroid	08	35	95	165	250
Anti D Ig	10	30	145	170	185
Eltrombopag	12	12	>25	>100	160

The incidence of chronic ITP is more in older children (>10 years of old).

DISCUSSION

The age ot the study population ranged from 9 months to 14 years (mean age 6.1± 1.5 yrs) which correlates with the studies of the International Childhood ITP Study Group and others.[19,20]

In our study there was slight female predominance, 36 (56%) female, 28 (44%) female, Male Female ratio was I : 1.3. This was similar to the studies done by Victor Blanchette et al.[19,21] in Hospital for the Sick Children, Toronto and others.

The platelet counts in our study subjects were 6000/cm to 1,25,000/cmm (mean 19000/cmm) which correlates with the study done by Watts RG in Children Hospital of Alabama, Bermingham.[19]

In our study the spontaneous remission rate was 25 (39%)) out of 64 patients which correlates with the study of Desiree Mediiros MD et al[22] but lower than the other studies.[19,23-25] The lower spontaneous remission rate in our patients might be due to starting of early corticosteroid by receiving junior doctors on admission of the patients in the Hospital. The spontaneous remission might be due to cessation of production as well as disappearance of responsible antibodies from circulation.

The response rate to corticosteroid was 26 (67%) out of 39 patient which correlates with studies of guideline for the American Society of Haematology and others (24,26) but lower than the study performed by Watts RG in Children Hospital of Alabama, Bermingham.[19] The mechanism of action of corticosteroid in ITP remains uncertain. Corticosteroid may inhibit the phagocytosis of antibody-coated platelets, may suppress antibody production in lymphocytes and may maintain capillary integrity.

The incidence of chronic ITP was 13 of 64 (20%) which is also close to the studies abroad.[19,25,29]

The response rate to Anti-D Ig was 100% maintaining platelet count >30,000/cm which is higher than the study by Watts RG.[19] and here IV Ig acts by competitive inhibition of monocyte/phagocyte systems affected by the preferential sequestration of autologous erythrocytes sensitized by alloantibody present in the Ig G preparations.[30]

The response rate to Eltrombopag was 5(71%) in 7 patient and maintaining platelet count >50,000/cmm which correlates with the studies done abroad.[31,32,33]

Chronic 1TP developed in older children in our study which had been shown in the studies performed by Watts RG.[19]

CONCLUSION

The overall prognosis in childhood ITP is excellent. Spontaneous response occurred in good number of cases (39%) and overall about 90% cases resolved with therapy or observation. Ant-Immunoglobulin and Eltrombopag are promising in chronic ITP though further larger study is needed.

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