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Clinical profile of immune thrombocytopenic purpua and outcome at 6 months: a South Indian observational study

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ABSTRACT

Background: Immune thrombocytopenia studies in South India is very limited. This study was carried out with an aim to find the clinical spectrum of immune thrombocytopenia and outcome of this disorder affecting the children of central Kerala and to assess whether the clinical spectrum and outcome of this disorder differs from the western population.

Methods: All newly diagnosed children of primary immune thrombocytopenia admitted in Paediatric ward from November 2012 to November 2013 were included in this study. Children with secondary causes of thrombocytopenia were excluded from the study population. Clinical profile and outcome at six months were studied. Children achieving complete response (platelet count $>100 \times 109/L$ and absence of bleeding) at six months was compared on the basis of severity of thrombocytopenia at presentation.

Results: Thirty children were studied. The common age group affected was ranging from two to six years. The incidence of intracranial bleed was 6.6% and mortality 3.3%. 75.8 % of patients attained complete response and 17.2% of patients had response at six months. No patients ended up in hematological malignancy in follow up.

Conclusions: Majority of patients with ITP does not require any intervention and only minor proportion of children progress to chronic immune thrombocytopenic purpura. Clinical spectrum and outcome of this condition does not differ from western studies. More research with larger sample size is required to study the incidence and outcome in Indian population.

Keywords: Immune thrombocytopenic purpura, Outcome of ITP, Profile of ITP, Spectrum of ITP

INTRODUCTION

Immune thrombocytopenic purpura (ITP) is one of the commonest causes of thrombocytopenia. Though it affects any pediatric age group, children between 2 to 6 years are commonly affected. 1.2 It is a benign disorder with good prognosis and outcome. Most patients of this disorder do not require any therapeutic intervention. Very small number of patients need therapeutic intervention due to profound thrombocytopenia and life-threatening bleeding. 1 Primary ITP is an autoimmune disease

characterized by platelet count $<100\times109/L$ in the absence of other secondary causes of thrombocytopenia.³ No consensus guideline available for management of this disorder and wide variations are found in clinical practice.⁴ ITP studies in South India is very limited.

This study was carried out with an aim to find the clinical spectrum of immune thrombocytopenia and outcome of this disorder affecting the children of central Kerala and to assess whether the clinical spectrum and prognosis of this disorder differs from the western population.

METHODS

This prospective observational study included all newly diagnosed children of primary immune thrombocytopenia admitted in Paediatric ward from November 2012 to November 2013. All cases were evaluated with proper history, clinical examination, complete blood count and peripheral smear. All children with secondary causes of thrombocytopenia were excluded from the study population.

Patients admitted with "life threatening bleeds" were treated with intravenous immunoglobulin 0.9 gm/kg/day, single dose, platelet transfusion and supportive measures.⁵ Children with platelet count less than 20,000/dl with overt bleeding or platelet count less than 10,000 with no bleeds were treated with intravenous immunoglobulin 0.8 to 1 gm/kg/day, single dose or prednisolone 4mg/kg/day for 4 days or inj. methyl prednisolone 30 mg/kg/day for 3 days followed by 20mg/kg/day for 4 days.⁵⁻⁷ All other patients were observed for 24 hours and no therapeutic intervention was done.

All patients included in the study were followed up and platelet count was done every month for 6 months. Those patients who were treated with IVIG or steroids had their platelet count monitoring at 12th hour, 24th hour, 72nd hour. All the investigations were done in medical college, laboratory.

The observations were entered in Microsoft excel spreadsheet and analyzed by statistical methods and P value was deduced to find the significance. The statistical packages used are SPSS 16 for the chi- square test. The results were recorded, and appropriate conclusions made.

Definitions and terminologies³

- Newly diagnosed ITP: within 3 months from Diagnosis
- Persistent ITP: between 3 to 12 months from diagnosis. Includes patients not achieving spontaneous remission or not maintaining complete response after therapy.
- Chronic ITP: lasting for more than 12 months
- Severe ITP: Platelet count less than 20 x 109/L irrespective of bleeds

Proposed criteria for assessing response to ITP treatment³

- Complete Response(CR): platelet count > 100 X 109/L and absence of bleeding
- Response(R): platelet count > 30 X 109/L and at least two-fold increase the baseline count and absence of bleeding
- No Response: platelet count < 30 x 109 /L or less than two-fold increase of baseline platelet count or bleeding.

RESULTS

During the study period, 30 patients of ITP were studied. Clinical profile of ITP and outcome at 6 months in all 30 patients were analysed.

Clinical profile

Children between 2 to 6 years comprise 60% (n=18) of the study population. Males constitute 73.3% (n=22) of the study population. 86.6% (n=26) of children had petechiae and purpura followed by ecchymoses (46.6%, n=14), oral bleeds (40%, n=12), epistaxis (6.6%, n=2), intracranial bleed (6.6%, n=2), hematuria (3.3%, n=1).

Seven children (23.3%) had history of preceding viral illness and one child who was aged one year, and three months received MMR vaccination 2 weeks prior to the onset of illness. Significant cervical and inguinal nodes were palpable in three children (10%). One child had mild splenomegaly. The incidence of intracranial hemorrhage was 6.6% (n=2).

Severe thrombocytopenia was noticed in 40% (n=12) of the study population. Eight children with atypical features (Three children had generalized lymphadenopathy, two children had leucopenia, one child had splenomegaly, two children with pallor disproportionate to bleeds) had undergone bone marrow examination. Megakaryocytic hyperplasia was demonstrated in four children and the remaining four showed no abnormality.

Among 12 patients who had severe thrombocytopenia, nine patients (30%) with significant bleeds required intervention. Out of nine, four children received intravenous immunoglobulin (IVIG), one child received parenteral methyl prednisolone, three children received oral prednisolone. A 12-year-old boy with intracranial bleed received both IVIG and methyl prednisolone because of no improvement. He expired after mechanical ventilation and intensive care unit stay of 17 days. All three patients treated with oral prednisolone achieved response at 72 hours whereas two children (50%) in IVIG group. No response was demonstrated in the only child who received both methyl prednisolone and IVIG at 72 hours.

Outcome at six months

22 children (73.3%) achieved complete response within six months. Among these 22 patients, 20 children (90.9%) achieved complete response in the first month. Five children (16.6%) achieved response at six months. Two patients (6.6%) had no response at six months. Both patients had no evidence of any mucocutaneous bleed at six months. Seven children were labelled as persistent ITP1 from three months onwards. In this study, 75.8% of patients achieved complete response at six months. The child who presented as intracranial bleed expired after 17 days. The mortality was calculated as 3.3%. Out of 12

children with severe thrombocytopenia at admission, seven (58.3%) achieved complete response at six months. Out of 18 children with mild and moderate thrombocytopenia at admission, 15 (83.3%) achieved complete response at six months. Out of 22 children who achieved complete response at 6 months, seven (31.8%) had severe thrombocytopenia at admission. Out of eight children who achieved no complete response at 6 months, five (62.5%) had severe thrombocytopenia at admission. The Chi square value was 2.301. The degree of freedom was one. P value was 0.12 (>0.05). Thus, statistically there was no significant difference between the two groups in achieving complete response at 6 months.

DISCUSSION

This study analyzed the clinical profile and outcome of ITP at 6 months

Clinical profile

In this study, the most common age group was 2-6 years accounting for 60% of the study population which is similar to various studies. 1.2 Kuhne et al demonstrated that affected mean age was 5.7 years. 2 In this study, male and female children constituted 73.3% and 26.7% respectively. This is in contrast to the study conducted by Kuhne et al which showed boys and girls are affected almost equally except male predominance in infancy. 2

In this study, the most common presentation of immune thrombocytopenic purpura was petechiae and purpura (86.6%) followed by ecchymoses (46.6%) which is in concordance with Choi et al and Bolton-Maggs et al study.^{8,9}

Out of 30 patients, seven patients (23.3%) had history suggestive of mild viral illness in the preceding 4 weeks in contrast to a review study by Blanchette et al which proved that two-third of cases were preceded by clinically apparent viral illness. One Child received MMR vaccination 2 weeks prior to the onset of immune thrombocytopenic purpura. The incidence of MMR (50%, n=1) associated immune thrombocytopenic purpura in this study is very high which is explained by the smaller sample size. According to the study conducted by Miller et al, the absolute risk within six weeks of immunization was one in 22,300 doses, with two of every three cases occurring in the six-week post-vaccination period being caused by MMR immunization.¹⁰

One 12-year-old patient required pediatric intensive care unit admission due to intracranial hemorrhage. Within 24 hours, he deteriorated and required mechanical ventilation. Two patients, one was previously mentioned and the other one was referred from a private hospital where he was treated with anti-convulsants for seizures following minor head trauma). Lee et al reported the incidence of intracranial hemorrhage in immune thrombocytopenic purpura was 3%. The higher

incidence of intracranial hemorrhage in this study (6.6%) was attributed to the smaller sample size.

60% of the study population were anemic. It was attributed to the prevalence of iron deficiency anemia in the community. All children responded to oral iron therapy. Leucopenia which improved after a week was observed among two children which was attributed to preceding viral infection. Peripheral smear showed neutrophilia in 26.6% of children, eosinophilia in 23.3% of children, relative lymphocytosis in 30% of study population. Blanchette et al described that eosinophilia is a common finding in immune thrombocytopenic purpura, though figures were not calculated and also noticed atypical lymphocytosis in some patients. Literature review revealed no neutrophilia in ITP children which was new finding in this study.

Non-tender cervical and inguinal lymph nodes were palpable in three patients (10%). Spleen was palpable two centimeters below left costal margin in a five-year-old child (3.3%). In all these four children, bone marrow showed normal erythroid and myeloid series with hyperplasia of megakaryocytes confirming immune thrombocytopenia. Choi et al described shotty cervical lymphadenopathy was common in young children and a spleen tip may be palpable in 5% to 10% of cases. Bone marrow examination was performed for eight children with atypical features. All of them were diagnosed as immune thrombocytopenia. Four of them had hyperplasia of megakaryocytes and the other four children showed normal erythroid, myeloid, megakaryocyte series.

In this study, among 30 patients, 12 children (40%) presented with severe thrombocytopenia. Out of 12, nine were treated and the other three children had no significant bleeds and observed for rise in platelet count.

Rate of rise in platelet was monitored in the initial 72 hours and compared among patients received intravenous immunoglobulin, methyl prednisolone and prednisolone. All three patients (100%) treated with oral prednisolone achieved response at 72 hours whereas two children (50%) out of four achieved response in IVIG group.² No response was demonstrated in the only child who received both methyl prednisolone and IVIG at 72 hours. Patients treated with oral prednisolone had quicker rise in platelet count compared to IVIG group which is not similar to several studies.^{1,5,6} Beck et al and several other studies proved that IVIG raises the platelet count in more than 80% of children and does so more rapidly than corticosteroids or no therapy.¹²

Outcome at six months

At six months, 22 patients (73.3%) achieved complete response. Five patients (16.6%) achieved response at 6 months. 2 patients (6.6%) had no response at 6 months. In this study, 73.3% of patients achieved complete response at 6 months. Several studies reported that, in 70-

80% of children who present with acute ITP, spontaneous resolution occurs within 6 months which is similar to this study.⁴ George et al reported 76% complete remission rate.¹³

In this study, out of 12 patients with severe thrombocytopenia, seven (58.3%) achieved complete response at six months. Out of 18 patients with mild and moderate thrombocytopenia, 15 (83.3%) achieved complete response at 6 months. Comparing the two groups by chi-square test (p value >0.05), there was no significant difference between patients with severe and non-severe thrombocytopenia in achieving complete response at 6 months. No previous studies have compared the outcome between these two groups.

One 12-year-old male patient expired due to intracranial hemorrhage after intensive care unit stay of 17 days. Mortality was calculated as 3.3%. Several studies show that mortality is less than 1%, though published reports of mortality in immune thrombocytopenia were limited. The mortality was high in this study because the sample size was very small.

The major limitation of this study was smaller sample size and patients were followed up only for 6 months.

CONCLUSION

ITP is a benign and self-limiting illness in most children. Majority of patients does not require any intervention. Most children achieve complete response by one month of disease onset. Clinical spectrum and outcome of this condition does not differ from western studies. More research with larger sample size is required to study the incidence and outcome in Indian population.

What is already known: ITP in children is well studied in western population.

What this study adds: Clinical spectrum and outcome of ITP in south India does not differ from western population.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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