International Journal of Contemporary Pediatrics
Champatiray J et al. Int J Contemp Pediatr. 2017 Jul;4(4):1470-1475
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20172688

Original Research Article

Evaluation of prevalence, clinical spectrum and outcome of acute ITP in children in a tertiary care centre in Odisha, India

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Received: 23 April 2017
Revised: 31 May 2017
Accepted: 03 June 2017

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ABSTRACT

Background: Idiopathic thrombocytopenic purpura (ITP), also known as immune thrombocytopenic purpura is one of the commonest bleeding disorders encountered in children between the ages of 2 to 10 years affecting both sexes. The objectives of the study were to collect the prospectively data including age, gender, bleeding type, platelet count and other laboratory tests, treatments, responses to treatment and outcomes in children with acute ITP from 1month to 14 years of age over a period of two years.
Methods: The present study was conducted in the Department of Paediatrics Shrirama Chandra Bhanj, Medical College and Hospital and Sardar Vallabhbhai Patel Post Graduate Institute of Paediatrics, Cuttack during the period October 2011-Septmber 2013.
Results: Total 36 cases of hospitalized acute ITP patients were studied out of 29200 cases. Prevalence of acute ITP was found to be 12.3 per 10,000 of all hospitalized children above 1 month. Male children outnumbered female children by Ratio 1.2. Past history of URTI was present in 78% of cases. Petechaie/purpura was the universal presenting features followed by Oral / Gum bleeding in 67% of cases. 8% of patient experienced clinical bleeding requiring blood transfusion and platelet transfusion. Mean duration of Hospital stay was 6.34 days. Maximum number of Patients (69%) had complete recovery and 14% each had persistent and chronic course.
Conclusions: ITP is a common pediatrics disease presenting at any age with low morbidity and mortality. Most children with acute ITP recover in weeks to months. A long-term hospital based prospective study is suggested to know any significant risk factor in patient presenting with acute ITP.

Keywords: Immune Thrombocytopenic Purpura (ITP), Tertiary Care

INTRODUCTION

Idiopathic thrombocytopenic purpura (ITP), also known as immune thrombocytopenic purpura is one of the commonest bleeding disorder encountered in apparently healthy children between the ages of 2 to 10 years affecting both sexes.[1] It has an incidence of 4.0-5.3 per 1 lakhs children.[2] There are 3 types of ITP- acute, chronic and persistent.[1] Acute ITP is a self-limiting condition with a peak incidence between 2 to 5 years of age, with 80 - 90% of uneventful recovery within 3 weeks to 6 months with or without specific treatment. Approximately 20% of children who present with acute ITP go on to have chronic ITP.[3] There are variety of manifestations such as mild symptoms like bruising, petechiae to severe symptoms like intracranial haemorrhage, retinal haemorrhage etc. Less than 1% children with ITP develop intracranial bleeds.[4]

Despite a great deal of research regarding ITP, the cause remains unclear. Immune mediated destruction of platelets is a major part of the pathophysiology, but the underlying mechanisms which trigger autoantibody production are poorly defined.[5]

At diagnosis, there are no known risk factors which predict the development of chronic disease in children. No variables are instructive in predicting response to therapy or bleeding risk. Identifying factors which are associated with chronic disease, response to therapy or bleeding risk would be invaluable in the treatment of this disease and would help guide the development of new therapies.

More than 80% of children with acute ITP can be managed without therapy and can be safely managed as outpatients with weekly visits.[6]

Some require specific treatment like glucocorticoids, methyl prednisolone, IVIG, Anti-D globulin, splenectomy etc. In October 2007, the International Working Group on ITP revised the terminologies to newly diagnosed ITP, persistent ITP and chronic ITP.

De Mattia et al found Chronic ITP occurs in about 20% of children, with a higher risk if >10 years and/or platelet count ≥20×109/L at presentation.[3]

Blanchette et al studied that about 37-50% of children with chronic ITP achieve remission within 4 years of diagnosis.[7]

The objectives of the study were to prospectively collect data, including age, gender, bleeding type, platelet count and other laboratory tests, treatments, responses to treatment and outcomes in children with acute ITP from 1month to 14 years of age over a period of two years, to perform descriptive analyses to define possible risk factors for chronic disease and to analyze outcomes, including treatment response and death.

METHODS

The present study was conducted in the Department of Paediatrics Shrirama Chandra Bhanj, Medical College and Hospital and Sardar Vallabhbhai Patel Post Graduate Institute of Paediatrics Cuttack during the period October 2011-Septmber 2013.

It was a prospective hospital based study which included the hospitalized children from 1 Month to 14 years of age. The total number of cases were 36.

Inclusion Criteria

All the children admitted with a clinical presentation, laboratory investigation and confirmed by bone marrow study as a case of acute ITP in the age group of 1 month to 14 years of either sex were included in this study.

Exclusion Criteria

New born bleeding cases, surgical condition or parents not given consent were excluded in my study.

A detail clinical history was taken in special reference to, associated family history of bleeding, history of fever, antecedent viral infection, history of diarrhoea, intake of drugs. Special attention was given to age of onset of bleeding, type of bleeding, site of bleeding, duration, frequency whether the bleeding was spontaneous or after intervention.

A thorough general examination of all children was done for anaemia, lymphadenopathy, sternal tenderness, hepatosplenomegaly. Skin was examined for petechiae, ecchymosis, and bruise. All the systemic examination including locomotor system which included examination of joints mobility, signs of inflammation, flexion deformities, were performed. Hess Test was done for dengue fever to look for petechiae. Appropriate laboratory investigations were done. All the cases were recorded in Performa as per the case recording form given in appendix. Findings thus obtained from clinical, laboratory evaluation analysed in tabular form.

After the definitive diagnosis, management of all cases were done according to standard regimen by Indian pediatrics3. All the cases were followed up by outdoor basis and outcome was noticed as per defining criteria by Indian pediatrics. Results were compared and co-related with observation similar study done by other workers. The data were noted in tabulate form. Necessary statistical procedures were applied using SPSS Version 21 and Microsoft Excel Software. It was used to observe the percentage of outcome variable in different demographic and clinical subgroups. Other parametric and nonparametric analysis, hypothesis verification was done as per necessity to arrive at a conclusion

RESULTS

This study included all patients admitted to the hospital between the study period according to the inclusion criteria and the total number of cases obtained were 29200 out of which 36 were confirmed cases of Acute ITP. This showed an incidence of 12.3 cases of diagnosed ITP per 10,000 admissions to the hospital.

As seen in Table 1, the age and sex distribution of the study group saw a predominance of 22 children aged 1month to 4 years with 63 percent of them being males. The 9 to 14-year-old group had predominantly females. Overall, out of 36 patients in the study group, 44 percent of them were females.

Table 2 shows the seasonal variation seen in the patient profile in our study which showed a majority 39 percent in the spring group.25 percent of the children were affected during winter season.

Table 1: Age and sex distribution in the study group (n=36).

Age groups	Sex		Total (n)
	Male	Female	
1 month to 4 years	4	8	22
>4 to 9 years	6	4	10
>9 to 14 years	0	4	4
Total	20	16	6

Table 2: Seasonal variation of patients in the study group (n=36).

Season	Number (n)	%	Cumulative percentage
Spring	14	38.9	38.9
Summe r	8	22.2	61.1
Rainy	5	13.9	75.0
Winter	9	25	100.0
Total	36	100.0	

Table 3 below shows the various patient characteristics that the patients were admitted with all 36 of the patients showed petechaie which formed the basis of the diagnosis. 11 to 22 percent showed other forms of bleeding like G.I bleeding, haematuria or menorrhagia. 5 out of the 36 patients had a palpable spleen. Only 5 percent of the children diagnosed had anaemia below 5gm% and around 8 percent each needed transfusion with either random donor platelet/ packed red blood cells. Most (72 percent) of the patients were hospitalised for 4 to 7 days for treatment and follow up.1 patient died due to severe intracranial haemorrhage. 78 percent of the patients had history of URTI. Table 4 shows the treatment given to each patient showing that most patients were given oral steroid in the form of oral omnacortil (prednisone) out of which 84 percent responded satisfactorily to the treatment. 2 patients were given Anti D at a dose of 50µg/kg IV as a single dose. All treatment arms did well with all groups attaining remission around 2 months post therapy according to Table 5 above. Also seen in the above table is that the platelet levels at presentation varied for each treatment arm, showing the lower platelet count at presentation receiving more aggressive treatment.

Table 6 clearly shows a significant difference between the age groups in the chronic ITP cases vs the Acute ITP.

Table 3: Characteristics of patients in the study group (n=36).

Clinical Presentations	No. of Patients (n=36)	%
Petechiae/purpura	36	100
Oral/gum bleeding	24	66.7
Epistaxis	8	22.2
Skin bleeding/ecchymosis	4	11.1
G.I bleeding	4	11.1
Haematuria	4	11.1
Menorrhagia	2	5.5
I.C.H	1	2.8
Palpable spleen	5	13.8
Haemoglobin		
<7	2	5.6
7-11	8	22.2
>11	26	72.2
Increased eosinophil count	8	22.2
Platelet count (at presentation)		
<10,000	3	8.3
10,000-20,000	8	22.3
>20,000	25	69.4
Required transfusion		
RDP	3	8.3
PRBC	3	8.3
No transfusion	30	83.4
Hospital Stay (no. of days)		
<4	2	5
4-7	25	69
>7	8	23
Past history		
URTI	28	77.8
Diarrhoea	6	16.7
Drug Intake	2	5.5

Table 4: Pattern of treatment and response in study group (n=36).

Treatment Given	Dose and duration	No. of Patients (n=36)	No. of patients responded	%
No treatment		3	2	66.7
Oral Omnacortil	1mg/kg PO×7day tapered over 3 weeks	13	11	84
Injectable Methylprednisolone	30mg/kg IV× 3d	9	4	44
IVIG	1gm/kg IV single dose	9	7	77
Anti-D	50µg/kg IV single dose	2	1	50

Table 5: Mean platelet levels in treatment groups at different time.

Treatment taken	Dose and duration	At time of presentation (1000/mm^3)	At 72 hr (1000/mm^3)	At 1 week (1000/mm^3)	At 2 months (lacs/mm^3)
No treatment		48300	63300	76600	1.03
Omnacortil	1mg/kg PO×7 days tapered over 3 weeks	34900	58500	73100	1.01
IV Methylprednisolone	30mg/kg IV×3 days	33600	60200	68300	1.01
IVIG	1gm/kg IV single dose	24200	70100	92500	1.12
Anti-D	50µg/kg IV single dose	24100	65100	90100	1.11

Table 6: Comparison of presenting features between chronic and acute group.

Variable	Outcome	N	Mean	Std. deviation	Std. error (mean)	P -value
Age	Chronic	5	9.50	1.26	0.565	0.0001
	Acute	31	3.94	2.54	0.455	
Hb	Chronic	5	9.42	2.19	0.981	0.0176
	Acute	31	11.53	1.69	0.305	
TPC	Chronic	5	41000	9055.4	4049.7	
	Acute	31	29806	13595.0	2441.8	0.0855
Gender	Chronic	5	1 male	4 females		0.0886
	Acute	31	19 males	12 females	-	

Patients presenting initially as acute ITP going on to Chronic ITP also had significantly lower Haemoglobin levels. There was no significant difference between the total platelet count between the chronic and acute ITP children. Also, no significant difference was found in the gender of the chronic and acute study groups.

Table 7: Outcome of the study group (n=36).

Outcome	No. of Patients	%
Complete recovery	25	69.4
Persistent	5	13.9
Chronic	5	13.9
Death	1	2.8
Total	36	100.0

Table 7 shows the outcome of patients admitted and diagnosed as acute ITP .14 percent each went on to be diagnosed as persistent ITP and chronic ITP. There was 1 death in the study group and 70 percent showed complete recovery.

DISCUSSION

This study included patients presenting over a period of 2 years from October 11 to September 13. All the patients included were stamped as cases of Acute ITP based on the clinical presentation, laboratory investigation and confirmed by bone marrow study. Out of total number of 29200 admitted patients to department of pediatrics in stated age group during the study period 36 cases were labeled as acute ITP basing on the defined criteria. So, prevalence of ITP in a tertiary care center of Odisha during two years of study is 12.3 per 10,000 admissions. However, study by Terrell et al shown incidence of 6.4 per 1,00,000 children but various authors like Zeller et al, Lilleyman JS had reported incidence between 1 to 6 per 1,00,000 per year which was lower than present study.[8-10] This difference may be due to small study population and for a short duration in comparison to other authors. Majority of cases 61.1% were observed in the age group of 1 month to 4 years followed by 27.8% in the age group 4 year to 9 years and only 11.1% belonged to age group greater than 9 years. Segal JB et al observed highest occurrence of acute ITP in the age group of 1-4 year.[11] In present study, the youngest being 11-months male child and eldest being 11 year 3 months. The mean age of presentation was 4.71 year with standard deviation ±3.067. Study by Watts RG showed mean age of acute ITP in children was 5.85 years with a range of 1 month-17years.[12] The ratio of male to female was 1.2:1. The slight male predominance in study tallies with the study by Segal JB et al.[11] However study by Lustre JM et al depicts equal distribution of cases in both the sex.[13] Maximum number of cases (38.8%) presented in the spring season, followed by winter (25%). Kuhne et al observed similar seasonal occurrence of acute ITP in children in their study.[14] This seasonal variation was must probable due to viral respiratory infection in the childhood during spring season. Upper respiratory tract infection was present in most (77.8%) of the cases, 6 patients (16.7%) had history of diarrhea, (5.5%) had history of drug intake. The occurrence of upper

respiratory tract infection, diarrhoea can be attributed to viral illness and culminating drug in two cases in this study was ibuprophen. These findings were similar to the observation by Oski et al.[15] Petechiae/purpura was universal finding in all (100%) cases, 67% cases had associated oral/gum bleeding, 22% of cases had associated epistaxis, haematuria was present in 11% of cases where as menorrhagia was found in 6% of cases and only one case (3%) had document intracranial haemorrhage. Similar pattern of presentation was reported by Blanchette et al.[16] Study of Lileyman JS showed incidence of intracranial haemorrhage is 0.2%.[17] The higher incidence in our study is due to small number of cases in our study.14% cases had associated splenomegaly in our study.

Lammi et al reported 12% cases of splenomegaly in children with acute ITP in his study.[18] Souid et al found 5-12% cases of splenomegaly in children in their study.[19] The occurrence of anaemia was 29%, out of which 6% case had severe anaemia (haemoglobin less than 7 gm%) and 23% had mild pallor that is haemoglobin 7-11 gm%. This finding was frequent in females more than 8 years of old. This could be due to associated iron deficiency anaemia and malnutrition in our state. George JN et al stated iron deficiency anaemia was found in ITP.[20] Marked eosinophilia in 22% of cases was present in this study. George JN et al reported eosinophilia may be a rare finding in acute ITP in children but the exact cause of eosinophilia is obscure.[20] The initial platelet count of the study group at the time of hospitalisation. 22.3% cases had platelet count in between 10,000-20,000 per mm3 and less than 10,000 per mm^3 platelet count was seen in 8.3% of cases. 69.4% had platelet count more than 20,000 per mm^3. Mean platelet count was 29640 per mm^3.

Current result matched with the study of George JN et al who opined in more than half of cases platelet counts at presentation are less than 20,000 per mm^3.[20] 8% cases required platelet transfusion and 8% cases required whole blood transfusion. All the transfusion groups had severe mucosal bleeding. Watts RG59 observed in his study that 6% patients had clinical bleeding requiring hospitalisation. The study finding tallies with the study of Watts RG.[21] 36.1% of cases were treated with oral omnacortil, 25% cases IVIG and 25% cases IV Methylprednisolone and 6% cases with Anti-D following standard guidelines. 8.3% cases were not treated with any medication and were kept under observation as per Indian paediatrics different therapeutic option exist for acute ITP.[3] Therefore, different patients in study group were administered different medication depending on their affordability and clinical profiles. There was rise of platelets in all treatment groups in 72 hours and 1 week, and after 2 month all the patients had platelet count more than 1 lakhs per mm^3. The p value is <0.1867. Blanchette VS et al in his study reported dramatic platelet response in children using high dose of IVIG.[16] A Canadian randomised trial by Blanchette and Carcao showed that the rate of platelet response was significantly faster in children who received treatment compared with those managed expectantly, for the end point of time (days) taken to achieve a platelet count greater than or equal to 20,000 per mm^3, IVIG and corticosteroids were equivalent, whereas IVIG was superior to oral corticosteroids therapy for the end point of time(days) taken to achieve a platelet count greater than 50,000 mm^3.[16] Though we observed platelet elevation in different times were similar in different groups, it was statistically insignificant and this could be due to lower study population. So, it needs a longer duration study for a definite conclusion.

The minimal hospital stay was less than 4 days in 5.7% and the maximum hospital stay that is more than 7 days in 22.9% cases and the maximum (71.4%) number of cases were hospitalised for 4 to 7 days. The mean duration of hospital stay was 6.34 days with minimum 3 days and maximum for 15 days. One patient died within 24 hours of admission. 25 patients (70%) had a complete recovery with platelet count more than 1, 00,000 per mm3. 5 children (14%) had persistent ITP that is low platelet count observed 3-12 months after diagnosis and 5 cases (14%) followed a chronic course. Only one case (3%) died in the study group, it was due to intracranial haemorrhage. Gadner H in his study observed complete recovery in 75-90% cases and chronic course in 10-25% cases and mortality in 0.1-0.5% cases.[22] De Mattia et al also found 20% of cases going for a chronic course.[3] The study finding is almost similar to the finding of above studies. The higher mortality in our case was due to small study population.

Response was seen 67% in no treatment groups, 68% cases treated with corticosteroids and 78% of cases treated with IVIG. There was no difference in response to any therapy. The p value is <0.9882 which is insignificant. Watts RG in his study in 510 children over 10 years found 100% response in no treatment groups, 92% response in corticosteroids group, 87% response in IVIG group and 91% response in Anti-D treated group.[21] The chronic ITP group had presentation at an older age (9.50 vs. 3.94 years for acute only p <0.0001), had higher initial platelet count (41000 vs. 29806 for acute only, p<0.0855) and low initial haemoglobin level (9.42 vs. 11.53 for acute only, p<0.0176). More number of females had chronic course (80% vs. 20%) in comparison to the acute ITP. Watts RG also observed occurrence of chronic ITP in children who had presented at an older age with higher initial platelet count.[21]

CONCLUSION

ITP is a common pediatrics disease presenting at any age with low morbidity and mortality. Most children with acute ITP recover in weeks to months. A long-term hospital based prospective study is suggested to know any significant risk factor in patient presenting with acute ITP.

ACKNOWLEDGEMENTS

Authors would like to thank for the help of the Superintendent and Head of the Department Dr. Saroj Kumar Satpathy in this endeavor for research and staff in the supervision and treatment of all the admitted patients. Authors gratitude towards the laboratory technicians without whom the above tests would not have been possible.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Champatiray J, Behera D, Krishnamoorthy A, Bhat S. Evaluation of prevalence, clinical spectrum and outcome of acute ITP in children in a tertiary care centre in Odisha, India. Int J Contemp Pediatr 2017;4:1470-1475.