

Management of Acute ITP in Children Fifteen Years' Experience

Jalil I Alezzi*

Pediatric Department, College of Medicine, Hadhramout University, Yemen

***Corresponding Author:** Jalil I Alezzi, Pediatric Department, College of Medicine, Hadhramout University, Yemen.

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Abstract

Objectives: To assess the outcome of Yemeni children with acute ITP who were not given any pharmacologic treatment and compared with those who were given in other studies.

Methods: A prospective observational hospital-based study was carried out between January 2002 to May 2016 at Al-Mukalla Maternity and Children Hospital and University Hospital for Mother and Child Health in Al Mukalla city/Hadhramout Governorate/Yemen, where 20 children with diagnosis of acute ITP. The diagnosis and classification of ITP were made according to the 2009 International Working Group criteria.

Results: Out of 20 children there were 11 males and 9 females, the ages range from 2 to 12 years. The mean age is 4.7 year with the median age at diagnosis was four years. The male: female ratio 1.6:1 below age of five; the median platelet count at time of presentation was 5000/ μ L. The remission rate in this study was 75% and 25% of them passed into chronic ITP.

Conclusion: The recovery rate has some relation with age at presentation and initial platelet count where young child and those with platelet count of < 20000/ μ L have better recovery rate. No any mode of pharmacologic treatment was given to affected children in the first six months of the illness.

Keywords: ITP; Children; Outcome; Management

Introduction

Immune thrombocytopenia (ITP) is defined by isolated thrombocytopenia (platelet count < 100,000/ μ L with normal white blood cell count and hemoglobin) [1-3]. Published data indicate that ITP is a benign condition for most affected children [4-7]. Intracranial hemorrhage (ICH) is the most serious consequence of ITP; fortunately it occurs in 0.1% - < 1% of patients [8-10]. There is no evidence that therapy prevent serious bleeding in children with ITP [11]. ITP can affect any age, but there is a peak incidence between two and five years, and the male/female ratio was highest in infants and decreased with age [12-14]. Children younger than 10 years of age are more likely to remit than older patients [1,13,15,16]. Data are limited in pediatric patients and indications for treatment are not standardized. Up to our knowledge there is no clear cut study which recommends withhold treatment in newly diagnosed ITP. Appropriate initial management may be either "watchful waiting" or pharmacologic intervention [2,17-19]. Most children with acute ITP do not require treatment, and ITP resolve spontaneously [5-7,18]. American Society of Hematology recommends that children who have no bleed or mild bleeding such as bruising and petechiae be managed with observation alone regardless of platelets count [19]. Up to 20 percent of affected children go on to have chronic ITP whether treated or not, which is defined as thrombocytopenia for more than 12 months since presentation [1,5,11,20,21]. Chronicity is increased with treatment especially methylprednisolone plus immunoglobulin [22].

Objectives

Primary objectives

1. To assess the outcome of children with acute ITP who were not given any pharmacologic treatment and compare with those who were given in other studies.

2. To show that there is no difference in the outcome whether to treat an acute ITP case or not.

Secondary Objectives

- 1- To assess the age and gender distribution among children affected by acute ITP.
- 2- To show the relationship of initial platelet count at presentation with the outcome of the diseases.
- 3- To show the relationship of age of the child at presentation with the outcome of the disease.

Patients and Methods

A prospective observational hospital-based study was carried out between January 2002 to May 2016 at Al- Mukalla Maternity and Children Hospital and University Hospital for Mother and Child Health in Al Mukalla city/Hadhramout Governorate/Yemen, where 20 children 11 males and 9 females, with diagnosis of acute ITP. The age ranges from 2 to 12 years. The defined age groups were 2 - < 5 year, 5 - < 8 years, and 8 - 12 years.

Inclusion criteria

1. Age less than 15 year.
2. Newly diagnosed ITP and who doesn't receive any pharmacologic treatment.
3. Approval by parents or caregivers.

Exclusion criteria

1. Any child with acute or chronic ITP who receives (d) any pharmacologic treatment.
2. Child with secondary ITP.

The diagnosis of ITP: The diagnosis and classification of ITP were made according to the 2009 International Working Group criteria [2], start with proper history and physical examination. Essential investigations include the followings: CBC and differential where platelet count below 100,000/ μ L was considered abnormal. Examination of the peripheral blood smear was conducted by a qualified hematologist who does not suggest other etiologies for the thrombocytopenia. Bone marrow aspiration was carried out under local anesthesia to all patients, to immediately exclude blood malignancies for patient or patient's family reassurance. The marrow result was hyper cellular, the erythroid and myeloid precursors were normal in number and appearance. The megakaryocytes were normal or increased in number, and some appear large. These findings are consistent with the diagnosis of ITP [23]. Other investigations like ANA, stool *H. pylori* Antigen, HBsAg, HCV antibody and HIV antibodies were done when indicated especially in chronic cases and all of them were negative. Antiplatelet antibodies test was not done for the patients in the study as it is not essential for diagnosis and many previous studies do not recommend it for suspected cases of ITP [17,21,22]. Fundoscopy was carried out when indicated and fortunately was clear. The only management prescribed in this study for of newly diagnosed ITP includes activity restriction, avoidance of antiplatelet and anticoagulant medications, regular monitoring of platelet count, and monitoring for clinical bleeding.

Newly diagnosed ITP – is an ITP within three months from diagnosis [1].

Chronic ITP is defined when the condition lasted more than 12 months [1,5,11,20,21].

Ethical consent

The study protocol was conducted according to principles of the Declaration of Helsinki, as well as reviewed and approved by the Ethical Research Committee at Hadhramout University/College of Medicine. The withholding of treatment option was thoroughly explained to the parents and caregivers of children involved in the study and their approval was obtained.

Statistical methods

The data were processed and analyzed by using computer and the data was analyzed by proportion and percentage. A p-value < 0.05 was considered significant, and the confidence interval was set at 95%.

Results

Out of 20 children there were 11 males and 9 females, the ages range from 2 to 12 years. The mean age is 4.7 year with the median age at diagnosis was four years. The male: female ratio 1.6:1 below age of five; while overall ratio was 1.2:1.

Table 1 shows the distribution of age group, gender and initial platelet count at the time of presentation, where the majority of affected children was below five and the median platelet count at the time of presentation was 5,000 (Inter-quartile range: 4000 - 20000/ μ L. Table 2 shows the relationship between initial platelet count and outcome of disease during follow up period, where those $\leq 10,000$ / μ L had achieved higher remission rate of 50%. Table 3 shows the relationship between age group at time of presentation and outcome of disease, where those below eight years old had achieved 65% remission rate. Table 4 Shows a comparison of the outcome of children with ITP in this study and other studies after 12 months of diagnosis. Ten patients (50%) were passed into remission with platelet count approaching $\geq 100,000$ / μ L in the first six months of the illness. Four children (20%) remit after one year of the illness. One child (5%) passed into remission after two years of the illness. The remaining five patients were followed after 6 months of the illness. First child (boy six years old) the platelet count ranged from 4000 to 10000/ μ L during follow up period of four years and still kept on no treatment although occasionally developed on/off petechiae and mild epistaxis especially after trauma, where nasal packing was used and reassurance was given. The second one (girl aged 10 years) her initial platelet count ranges from 10000 - 20000/ μ L developed on/off gum bleed and epistaxis, after four year of follow up the family insist on treatment, so she was prescribed Immunoglobulin iv four months later she developed another attack of bleed and given course on prednisolone for two weeks then tapered, at sixth year of follow up she is still having platelet count around $\leq 50,000$ / μ L. The third one (boy aged 12 years) had platelet count above 50,000 but less than 100,000/ μ L and fortunately had no bleeding episodes during following period of six years. The fourth child A girl aged 8 years had platelet count ranged from 20,000 to 30,000/ μ L with occasional mild gum and skin bleeding, she was followed up for four years her platelet count ranged from 50000 - < 100000/ μ L with no reported episode of bleed. The fifth child (girl seven year old) got platelet count $\leq 50,000$ / μ L after 6 years following the illness with occasional petechiae and no major episode of bleed.

Age group (in years)	Gender		Initial platelet count/ μ L
	Male	Female	
2 - < 5	8 (40%)	5 (25%)	4000 - 10000
5 - < 8	2 (10%)	2 (10%)	5000 - 20000
8 - 12	1 (5%)	2 (10%)	10000 - 20000
Total	11 (55%)	9 (45%)	

Table 1: Distribution of age group, gender and initial platelet count at time of presentation of children with acute ITP.

P value < 0.05 df = 1 chi sq. 9.926

Initial platelet count/ μ L	Outcome		Follow up period
	Remission	Not	
4000 - < 10000	10 (50%)	1 (5%)	3mo. - 4 yr.
10,000 - < 20000	4 (20%)	2 (10%)	1yr.- 6 yr.
≥ 20000	1 (5%)	2 (10%)	2yr.- 8 yr.
Total	15 (75%)	5 (25%)	

Table 2: The relationship between initial platelet count and outcome of disease during follow up period of children with acute ITP.

P value < 0.05 df=1 chi sq. 16.0

Age group (in years)	Outcome	
	Remission	Not
2 - < 5	9 (45%)	0
5 - < 8	4 (20%)	2 (10%)
8 - 12	2 (10%)	3 (15%)
Total	15 (75%)	5 (25%)

Table 3: The relationship between age group at presentation and Outcome of children with acute ITP.

P value < 0.05 df=1 chi sq. 15.485

This study (Yemen) 2016		(Argentina) 2009 [28]		(Saudi Arabia) 2012 [29]		(Canada) 2010 [30]	
Remission	Not	Remission	Not	Remission	Not	Remission	Not
75%	25%	71.3%	28.7%	70%	30%	80%	20%

Table 4: Shows comparison of outcome of children with acute ITP in this study and other studies after 12 months of diagnosis.

P value > 0.05

Discussion

ITP is a benign condition affecting children of different age groups, the majority of affected children in this study were below five years of age which is in agreement with other studies [12-14], probably these age groups are more likely to expose to viral illnesses and vaccination. In childhood ITP, there is a slight preponderance of boys, especially in infants. In this study the male/female ratio was 1.6:1 in the age group below five probably being a male is a risk factor and almost equal after this age, which is similar to what was seen in other studies [12,13]. Platelet counts in children are generally somewhat lower than in adults with ITP. In this study the initial platelet count of $\leq 10000/\mu\text{L}$ was found in 65% of affected children, this is in agreement with that found by Kühne and Rosthøj [13,23]. The majority of affected children recover from ITP (i.e. platelet count increases to $> 150,000/\mu\text{L}$) within three to six months of presentation, with or without treatment [5-7,13,18,23]. In this study the affected children didn't given any mode of therapy during first six months of the illness and observed closely during this period for any major bleed, fortunately no life-threatening bleeding occurred, and no patient died. No one of them develop ICH or gastrointestinal bleed, but they developed mild skin and mucus membrane bleeds with epistaxis which was treated conservatively and reassurance of the child and the family. Initial low platelet count ($\leq 10000/\mu\text{L}$) is not frightening to the clinician and to the family as it is associated with high remission rate It was found in previous studies that initial low platelet count ($\leq 20000/\mu\text{L}$) and children below 10 years of age at presentation have the higher remission rate [2,8,13,24]. In this study the remission rate was 70% in those with platelet count $< 20000/\mu\text{L}$, while the affected young children had a higher remission rate in comparison to older ones (65%), since older children tend to develop chronic ITP [2,8,13,24]. Regarding the remission rate, there is no significant difference between this study (just observation and no pharmacologic treatment) and others studies [25-27], as shown in table 4, *P value > 0.05*, so there is no need to start pharmacologic therapy depending on the initial platelet count or mild petechiae and some mucus membrane bleeds or even epistaxis.

Conclusion

ITP in children is a benign condition and should be treated conservatively irrespective of initial platelet count, most common age group affected was \leq five with a male: female ratio was 1.6:1. But overall ratio was 1.2:1. No any mode of pharmacologic therapy was given to the affected children in the first six months of the illness. The remission rate in this study was 75% and 25% of them (mostly females) passed into chronic course of the disease.

Recommendations

From this study we can recommend the followings:

1. Withhold pharmacologic treatment in childhood ITP at least in mild to moderate cases and watchful waiting is the best choice for ITP management irrespective of initial platelet count.
2. Although bone marrow aspirate done to all patients in this study, it can be omitted safely from the investigations in straightforward cases of ITP, in suspected cases one can do antiplatelet antibody if it available, to support the suspicion.
3. Telling the parents or care-giver about the prognosis of the ITP depending upon the age at presentation and initial platelet count.
4. Further studies are advised to confirm the findings of this study and to put a standardization of ITP treatment in children.

Disclosure

Author have no conflict of interests, and the work was not supported or funded by any drug company.

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