Original Research

CLINICAL AND HEMATOLOGICAL FEATURES OF CHILDHOOD IMMUNE THROMBOCYTOPENIA AT PEDIATRIC CENTER OF HUE CENTRAL HOSPITAL

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ABSTRACT

Background: *Immune thrombocytopenia (ITP) is the most common of the hemorrhagic diseases caused by thrombocytopenia in children. It usually occurs between the ages of 5 and 7 years old and at both sexes. It is difficult to predict ITP basing on bleeding because some severe thrombocytopenia cases have slight purpura or ecchymoses. This study aims to describe the clinical and hematological features of childhood immune thrombocytopenia*

Methods: *This was a cross - sectional study. Patients were stratified according to age (0 to 15 years) and diagnosed ITP at the Pediatric Center of Hue central Hospital.*

Results: *From May 2020 to March 2021, we identified 42 children diagnosed with idiopathic thrombocytopenia. Newly diagnosed ITP was the most common (66.7%) followed by chronic ITP (26.2%) and persistent ITP (7.1%). There was a slight predominance of boys to girls with the male - to - female ratio was 2:1. However, this ratio was dependent on ITP phases. The highest prevalence of immune thrombocytopenia was found under 6 years old. Children in this study usually had a history of preceding infection or vaccination. Natural hemorrhage was 83.3% (skin 95.2%). The most common type of cutaneous bleeding was petechiae (83.3%). Mild to moderate hemorrhages were dominant. Newly diagnosed ITP had less severity of hemorrhage than persistent and chronic ITP. Most children did not have a fever, hepatomegaly, splenomegaly, and lymphadenopathy. The majority of children seem to have severe thrombopenia (66.7%), but the number of platelets was not related to the severity of bleeding. Mean platelet volume was normal.*

Conclusions: *Newly diagnosed ITP was the most common. There was a little clinical and hematological features difference between the ITP phases.*

Keywords: *Immune thrombocytopenia, children, clinical features, hematological features.*

I. BACKGROUND

Immune thrombocytopenia (ITP) is a disorder characterized by accelerated destruction of antibody sensitized platelets by phagocytic cells, especially those of the spleen. In many affected individuals, inhibition of megakaryopoiesis also contributes to the degree of thrombocytopenia. ITP is the most common autoimmune disorder affecting a blood element. The annual incidence is about 1 in 10,000 children [1].

ITP formerly has many other names such as idiopathic thrombocytopenia, primary thrombocytopenic purpura, isolated

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thrombocytopenic purpura... It usually occurs between the ages of 5 and 7 years old and at both sexes [2,3].

Acute ITP is usually a benign, self - limited condition that occurs in young children, typically those younger than 10 years. Acute ITP usually onset after previous viral infection or vaccination. In most of these patients, the thrombocytopenia resolves within weeks or a few months of the original manifestation. Chronic ITP is defined arbitrarily as the persistence of thrombocytopenia (platelet count < 150,000/μL) for longer than 12 months after the initial manifestation [1].

It is difficult to predict ITP basing on bleeding because some severe thrombocytopenia cases have slight purpura or ecchymoses. However, severe bleeding may also occur in infants, including gastrointestinal bleeding, hematuria, and, rarely, intracranial hemorrhage. The rate of intracranial hemorrhage in children ranges from 0.1 to 0.4% [4 - 6].

In addition, ITP greatly affects the quality of life, especially in the first year after diagnosis. Factors affecting the child's life are the limitation of activities, concerns, worries because of the risk of bleeding in the future, and the process of treatment, follow - up, re - examination is not unified [7, 8]. The disease has a variety of clinical manifestations, diagnosis is based only on clinical and some simple tests without a gold standard. Therefore, the role of the clinician in the examination and evaluation of test results is very important in making a correct diagnosis [9 - 12]. We conducted a study to describe the clinical characteristics and hematological changes in childhood ITP and determine some relationships between clinical characteristics, hematological changes with ITP phases.

II. MATERIALS AND METHODS

2.1. Subjects

There were 42 childhood ITP patients diagnosed and treated at the Pediatric Center of Hue Central Hospital of Vietnam from May 2020 to March 2021.

2.2. Eligibility Criteria

In a child with the typical hemorrhagic presentation of ITP (sudden appearance of petechiae or ecchymosis in a healthy child), the diagnosis is established based on the following criteria [10]: Platelet count < 100,000/μL. Red blood cells and white blood cells in complete blood count are normal. There is no history and physical examination to suggest another cause ofthrombocytopenia.

2.3. Exclusion criteria

- The child has recently received a red blood cell transfusion within the last 3 months, platelet transfusion within the last 1 week.

- The patient's parents did not consent to participate in the study.

2.4. Method

Study design: a cross - sectional study

Data collection: pre - designed questionnaires and research records were collected from the medical records at the department.

Definition of research variable: ITP is divided into three phases [2]: (1) Newly diagnosed ITP: within 3 months from diagnosis. (2) Persistent ITP: between 3 to 12 months from diagnosis. Includes patients not reaching spontaneous remission or not maintaining complete response off therapy. (3) Chronic ITP: lasting for more than 12 months.

The bleeding scale for pediatric patients with ITP is presented in **Table 1**

Table 1: Bleeding scale for pediatric patients with ITP [12].

Grade	Bleeding
Grade 1 (minor)	Minor bleeding, few petechiae (≤ 100 total) and/or ≤ 5 small bruises (≤ 3 cm in diameter), no mucosal bleeding
Grade 2 (mild)	Mild bleeding, many petechiae (> 100 total) and/or > 5 large bruises (> 3 cm in diameter), no mucosal bleeding
Grade 3 (moderate)	Moderate bleeding, overt mucosal bleeding, troublesome lifestyle
Grade 4 (severe)	Severe bleeding, mucosal bleeding leading to decrease in Hb > 2 g/dL or suspected internal hemorrhage

2.5. Statistical analysis

We used the software SPSS 18.0 to analyze the data by medical statistical method.

Using general statistical algorithms, calculate the mean, median, and standard deviation of the obtained parameters.

Using the t - student test method to compare the mean between two independent, normally distributed groups. The Mann - Whitney test was used to compare the mean between two non - normally distributed groups. Use one - way Anova test when comparing more than 2 mean values normally distributed and uniform variance. Use the Kruskal - Wallis test when comparing more than two means when the variable is not normally distributed. Use the χ^2 test to test the difference of the ratios. Fisher correction when > 20% of cells have an expected value less than 5.

In all testing methods, $p < 0.05$ is statistically significant.

2.6. Research ethics

The study was approved by the Research Ethics Committee of Hue Central Hospital.

III. RESULTS

The epidemiological features are listed in **Table 2**. In general, boys were more common than girls (male to female ratio was 2:1). Boys predominated in the persistent and chronic phases. While the percentage of young children in ITP accounted for the majority, the proportion of older children in persistent and chronic ITP was predominant.

Table 2: Epidemiological features of patients with ITP

Features		Newly diagnosed ITP (N = 28)	Persistent ITP (N = 3)	Chronic ITP (N = 11)	p
Sex, n (%)	Male	23 (82.1)	1 (33.3)	4 (36.4)	0.008
	Female	5 (17.9)	2 (66.7)	7 (63.6)	
Age, n (%)	< 1 year - old	14 (50.0)	0 (0)	0 (0)	< 0.001
	≥ 1 - < 6 year - old	10 (35.8)	2 (66.7)	2 (18.2)	
	≥ 6 – < 10 year - old	2 (7.1)	0 (0)	5 (45.5)	
	≥ 10 year - old	2 (7.1)	1 (33.3)	4 (36.4)	
	Median (25th - 75th)	0.9 (0.3 - 2.7)	2.5 (2.4 - 9.1)	8.2 (6.3 - 12.6)	0.001

Table 3 shows the clinical features of childhood ITP. Children with ITP often bleeded due to minor injuries (83.3%), petechiae, or ecchymosis (83.3% and 57.1%, respectively). There were 42.9% of ITP children with mucosal bleeding, 9.5% of children with gastrointestinal bleeding. The most common bleeding scales were mild (38.1%) and moderate (35.7%). 42.9% of children with ITP had a history of infection and 38.1% had a history of vaccination within the past 6 weeks.

Table 3: Clinical features of childhood ITP

Features		Number	Percentage
Bleeding situation	Minor injuries	36	85.7
	Major injuries	6	14.3
Skin bleeding	Petechiae	35	83.3
	Purpura	6	14.3
	Ecchymosis	26	61.9
Mucosal bleeding	Epistaxis, intra - oral bleeding, gingival bleeding	17	40.5
	Menorrhagia	1	2.4
Gastrointestinal bleeding		4	9.5
Bleeding scale	Grade 1 (minor)	6	14.3
	Grade 2 (mild)	16	38.1
	Grade 3 (moderate)	15	35.7
	Grade 4 (severe)	5	11.9
History	History of infection within the past 6 weeks.	18	42.9
	History of vaccination within the past 6 weeks.	16	38.1
	Allergy	3	7.1
	Congenital defects	0	0.0
	Family history of hemorrhagic and/or allergic disease	9	21.4

Children with newly diagnosed, and chronic ITP had lower platelet counts than persistent ITP. There was no statistical difference in platelet volume, degree of anemia and white blood cell count among ITP phases **(Table 4)**.

Table 4: Hematology features in childhood ITP

Features		Newly diagnosed ITP (N = 28)	Persistent ITP (N = 3)	Chronic ITP (N = 11)	p
Platelet n (%)	< 20 x 10^9/L	20 (71.4)	1 (33.3)	7 (63.6)	< 0.05
	20 - 50 x 10^9/L	7 (25.0)	0 (0)	4 (36.4)	
	> 50 x 10^9/L	1 (2.4)	2 (66.7)	0 (0)	
	Median (25th - 75th)	15.0 x 10^9/L (13.0 - 27.0)	53.0 x 10^9/L (33.0 - 69.5)	18.0 x 10^9/L (5.5 - 32.5)	< 0.05
Mean platelet volume n (%)	< 6 fL	8 (28.6)	0 (0)	4 (36.4)	> 0.05
	6 - 9 fL	7 (25.0)	2 (66.7)	4 (36.4)	
	> 9 fL	13 (46.4)	1 (33.3)	3 (27.3)	
	mean ± SD	8.5 ± 3.1	8.9 ± 1.8	7.5 ± 2.7	> 0.05
Anemia severity n (%)	No anemia	14 (50.0)	2 (66.7)	6 (54.5)	> 0.05
	Mild	4 (14.3)	0 (0)	2 (18.2)	
	Moderate	10 (35.7)	0 (0)	3 (27.3)	
	Severe	0 (0)	1 (33.3)	0 (0)	
White blood cells n (%)	< 10 x 10^9/L	16 (57.1)	2 (66.7)	7 (63.6)	> 0.05
	≥ 10x 10^9/L	12 (42.9)	1 (33.3)	4 (36.4)	

IV. DISCUSSION

4.1. Epidemiological features

During the period from May 2020 to March 2021, a total of 42 cases of pediatric patients were diagnosed with ITP at Hue Central Hospital. Among them, there were 28 males (66.7%) and 14 females (33.3%), the male to female ratio is 2:1, showing that boys dominate. When compared with the male to female ratio in other studies, the male:female ratio in our study was higher [13, 14]. **Table 2** showedthat in the newly diagnosed ITP, the number of male was much higher than the number of female, but when looking at the persistent and chronic ITP, this was the opposite, females predominated over male children. This difference was statistically significant ($p = 0.008$). This suggested that boys were more dominant in the newly diagnosed ITP while girls were more common in the persistent and chronic ITP.

Regarding age, the average age of the study subjects was 4.5 ± 4.9, mainly in the under 6 age group **(Table 3)**, this was the age group prone to infectious diseases. Studies by Watts RG, Sutor AH, Kühne T showed that the age of the disease and the distribution of children by age group were similar to our results [15 - 17]. Regarding the age according to ITP phases, **Table 2** showed that most of the newly diagnosed phaseswere at a young age while the chronic form was in older children ($p < 0.001$), in terms of the median age of children in 3 ITP phases also showed a statistically significant difference ($p = 0.001$). This was also consistent with the literature, cases of newly diagnosed ITP were often related to respiratory or gastrointestinal infections, whereas chronic ITP was often related to immune system disorders in older children and adults [16, 17].

Regarding the phase of ITP, newly diagnosed ITP accounted for the most with 66.7%, persistent 7.1%, and chronic 26.2%, consistent with published reports [17, 18].

4.2. Clinical features

Childhood ITP usually begins after viral infection, vaccination... within 1 - 6 weeks or without any special history. Most children have generalized bleeding after minor injuries, with many different shapes and locations. In addition to features of hemorrhagic signs, children are usually healthy [11, 14].

Regarding the hemorrhagic morphology, the results of **Table 3**, showed that the petechia predominates with 83.8%, the forms of purpura, ecchymosis, mucosal bleeding from the nose, gums, and throat, gastrointestinal bleeding accounted for 14.3%, 57.1%, 40.5%, 9.5%, respectively. According to Paula Bolton's study on bleeding symptoms of 427 children, ecchymosis accounted for the majority with 90.4%, petechia or purpura accounted for 72.6%, epistaxis accounted for 19.9%, bleeding in the mouth, gums, tongue 15.9%, gastrointestinal bleeding 2.3%, hematuria 1.4%, menorrhagia 0.7% [19]. This difference may be due to the sampling method, sample size, and geographical location of the study.

Mild bleeding accounted for the most proportion with 38.1%. The majority of hospitalized children with ITP had mild to moderate bleeding (70.3%), similar to Zeller B's study with 97% [14].

Table 3 shows that 42.9% of children had a history of infection within 6 weeks and 38.1% of children had a history of vaccination within 6 weeks. Infectious factors and vaccination had been mentioned in many articles, Zeller B's study showed that more than half of pediatric patients had an infection within 4 weeks before being diagnosed with ITP [14], according to Paula Bolton 57% had ITP previously triggered by viral infection or vaccination [19].

4.3. Hematology features

Regarding the platelet count, among the 42 children, 66.7% of the patients had a platelet reduction of less than 20×10^9/L, accounting for the majority. The mean platelet count was 21.8 ± 18.3 x 109/L. Studies in the world had shown that most of the platelet counts are severely decrease [14, 15, 18, 20].

Regarding the anemia severity, in our study, it was found that no anemia accounted for the majority with the rate of 52.4%, the degree of severe

anemia was 2.4%, accounting for the lowest rate, mild and moderate anemia have rates of 14.3% and 31.0%, respectively. In Paula Bolton's study, 3.0% of children had hemoglobin levels below 10g/dL [19]. There was no statistical relationship between the degree of anemia and disease phases ($p > 0.05$). The degree of anemia distribution was quite similar in the disease phases, there was no statistically significant difference.

Table 4 showed that the newly diagnosed and chronic ITP had more severe thrombocytopenia than the persistent ITP, and the mean platelet count of the persistent ITP was much higher than that of the other ITP phases, this difference was statistically significant ($p < 0.05$).

Regarding the platelet volume, **Table 4** showed that the mean platelet volume was within the normal value with similarity in all three ITP phases, there was no statistically significant difference ($p > 0.05$). Regarding the distribution of platelet volume, there was no difference between the ITP phases ($p > 0.05$). Thus, in ITP, it seems that the platelet volume does not change.

Regarding the white blood cell count, the percentage of children with a white blood cell count of more than 10 x 10^9/L accounted for 40.5%.

V. CONCLUSION

In this study, it was noted that ITP is common in boys, with a male/female ratio of 2/1. However, the male/female ratio varies according to the disease phase, with the newly diagnosed form of the disease having a male predominance while the persistent and chronic form was the opposite.

ITP was characterized by hemorrhagic syndrome, skin bleeding was the most common clinical manifestation with over 90% of cases, most of which were spontaneous bleeding, with a small percentage of gastrointestinal bleeding. The degree of bleeding from light to moderate accounted for a large proportion, affecting more or less the quality of life of children, in the newly diagnosed phase, there was a lighter level of bleeding than in the persistent and chronic phase. Infections and vaccinations were commonly found in the study subjects.

About hematological features, most children had a severely reduced platelet count, but there was no relationship between the degree of thrombocytopenia and the degree of bleeding. The study also showed that there was no difference between the platelet volume in different ITP phases and it seemed to be a normal value.

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