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Clinical and Laboratory Characteristics of Newly diagnosed versus Chronic Primary ITP Children in a Tertiary Center

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ABSTRACT

Background: Immune thrombocytopenia is the most common acquired bleeding disorder in children, characterized by isolated thrombocytopenia with otherwise normal hematologic parameters. The clinical course varies from transient, self-limiting thrombocytopenia to chronic, treatment refractory disease. Comparative characterization of newly diagnosed and chronic pediatric ITP may provide insights into disease behavior and management trends.

Aim: To compare the clinical presentation, laboratory parameters and treatment strategies between newly diagnosed and chronic pediatric primary immune thrombocytopenic patients in order to identify potential differences that may influence disease understanding and management.

Patients and methods: This comparative cross sectional study included 25 newly diagnosed ITP children (Group A) and 25 children with chronic ITP (Group B). Our patients were selected from Pediatric Hematology and Oncology Unit, Minia University Children Hospital. Participants underwent medical history, clinical examination and complete blood count. Demographic data, clinical parameters, treatment modalities and laboratory findings were analyzed.

Results: The mean of age among the studied groups showed a statistically significant difference with chronic ITP patients being notably older (10.3 ± 2.44 years) than those of newly diagnosis (7.64 ± 1.97 years),$p<0.001$. Chronic ITP patients demonstrated significantly higher use of thrombopoietin receptor agonists (44% vs. 16%, $p = 0.006$). Patients of chronic group exhibited lower hemoglobin levels compared to newly diagnosed group (10.5 ± 0.87 vs. 11.0 ± 0.80 g/dl, $p = 0.043$) and higher platelet counts (28.1 ± 7.67 vs. 12.3 ± 5.72 × 10^3/ml, $p < 0.001$). Both groups exhibited similar bleeding patterns, with purpura and ecchymosis as the predominant manifestations, and no significant difference in bleeding severity ($p = 0.571$). Total leukocyte counts showed no significant differences among studied groups. Sex distribution in both groups did not differ significantly (60% males in Group A vs. 44% in Group B, $p = 0.258$). Similarly, positive consanguinity showed no significant difference (44% vs. 40%, $p = 0.774$)

Conclusion: Our study concluded that the mean age of children with chronic ITP was significantly higher than that of those with newly diagnosed ITP. Therapeutic patterns differed significantly, with corticosteroids and IVIG being the mainstay in newly diagnosed cases, while thrombopoietin receptor agonists were predominantly used in chronic disease. Chronic ITP patients had significantly lower hemoglobin levels, while platelet counts were higher. Study groups presented mainly with cutaneous bleeding but severe hemorrhagic events were absent.

KEYWORDS: Primary Immune Thrombocytopenia, Children, Clinical Features, Laboratory Parameters.

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INTRODUCTION

Backgrounds

Immune thrombocytopenia (ITP) of childhood is an acquired immune-mediated, and usually self-limiting condition of low platelet counts (< 100,00/µL). Newly diagnosed ITP refers to ITP up to 3 months after diagnosis. Persistent ITP refers to ITP lasting between 3–12 months from diagnosis, Chronic ITP is reserved for patients with ITP lasting >12 months, about 20–30% progress to chronic ITP, which is associated with greater morbidity, need for second-line therapies, and reduced health-related quality of life **(1)**.

Primary ITP is thrombocytopenia without a known cause. This occurs when immune system attacks platelets. It is caused by antibodies (mostly immunoglobulin G [IgG]) directed against antigens normally present on platelet membranes such as glycoproteins IIb/IIa and Ib/IX . About 80% of all cases are primary ITP. Secondary ITP: This may happen if underlying

conditions like chronic infections, blood cancers or autoimmune disorders affect platelet levels **(2)**.

The worldwide incidence of ITP in children is ~4–8 per 100 000 person per year **(3)** , Boys are more likely than girls to be affected **(4)**. The condition often follows a viral prodrome and presents predominantly with mucocutaneous bleeding (e.g., petechiae, purpura, ecchymoses) ranging from mild to moderate, whereas life-threatening hemorrhage remains rare. ITP is a diagnosis of exclusion, key considerations include the patient's medical history, physical examination, complete blood count and peripheral blood smear **(5)**.

Early treatment does not alter the natural course and does not affect the development of chronic ITP. The same principles of treatment of acute ITP apply to a certain extent to management of chronic ITP **(1)**. American Society of Hematology guidelines **(2019)** recommend: No treatment if the child has few or no symptoms.When therapy is indicated, the primary treatment options are Corticosteroids, Intravenous immunoglobulin (IVIG) and Intravenous anti-D Ig. In children with ITP who do not respond to first-line treatment, guidelines recommend the use of thrombopoietin receptor agonists (TPO-RAs) rather than rituximab **(6)**. Splenectomy is an effective therapeutic option for children with chronic ITP. Recently, TPO-RAs and rituximab have been preferred, and splenectomy is performed less frequently **(7)**.

However, an increasing number of children with chronic or refractory disease receive TPO-RAs and other second-line options. Yet, despite recent advances, a significant gaps persist in understanding the transition from newly diagnosed to chronic ITP in children, the comparative clinical and hematological profiles of these phases, and the impact of therapeutic interventions on disease course and laboratory parameters. While individual studies have addressed predictors of chronicity (e.g., older age, female sex, insidious onset) in pediatric cohorts, comprehensive comparative analyses of newly diagnosed versus chronic ITP remain limited.

Therefore, the present study was undertaken to compare the clinical, hematological, and therapeutic characteristics of newly diagnosed versus chronic pediatric ITP patients in a single-centre cohort, in order to identify distinguishing features associated with disease chronicity and to inform tailored management strategies.

PATIENTS AND METHODS

This prospective-cohort study included 25 newly diagnosed ITP children (Group A) and 25 children with chronic ITP (Group B). Our patients were selected from Pediatric Hematology and Oncology inpatient ward and outpatient clinic, Minia University Children Hospital, during the period from December 2023 to October 2024.

Inclusion Criteria: Children age range (5-15 years) of both sex with primary immune thrombocytopenia (platelet count of <100 $x10^9$/L) according to ASH guidelines **(6)**

Exclusion Criteria: Children with thrombocytopenia due to other known causes such as autoimmune conditions (e.g. SLE), medications, lymphoproliferative diseases (e.g. chronic lymphocytic leukemia) and Chronic infections **(2)**. Children with Inherited thrombocytopenia also excluded.

Participants underwent medical history, clinical examination and CBC. Demographic data, clinical parameters, treatment modalities and laboratory findings were analyzed. Bleeding severity was assessed using the Pediatric ITP Bleeding Scale (IBLS) .

- Pediatric ITP Bleeding Scale (IBLS) (8) :

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

Ethical Consideration :
All participant information is treated with the utmost confidentiality. In no publication or report will the names of the study's participants appear. All participants were informed of the study's goals, methodology, and risk-benefit analysis before their enrollment. The subjects gave their informed permission.

Ethical Approval:
The study was approved by the Ethics Committee of Minia University Faculty of Medicine. Written informed consent was obtained from all participants' guardians in accordance with the Declaration of Helsinki.

Statistical Analysis :
The analysis of the data was carried out using the IBM SPSS 26.0 statistical package software (IBM; Armonk, New York, USA). Normality of the data was tested using the Kolmogorov-Smirnov tests. Data were expressed as mean and standard deviation, minimum and maximum of range for quantitative measures, in addition to both number and percentage for categorized data. Mann-Whitney U test for non-parametric data were used for comparison between two independent group and Kruskal-Wallis test used for comparison between multiple independent groups among the non-parametric data. Wilcoxon Test for comparison of two related groups. The *Chi-square test or Fisher's exact test* were used to compare categorical variables. A p-value less than 0.05 was considered significant.

RESULTS

Table 1: Comparison between studied groups regarding demographic data.

Demographic data	Newly diagnosed ITP (A) (N = 25)	Chronic ITP (B) (N = 25)	p value
Age (years): **Mean ± SD**	7.64 ± 1.97	10.3 ± 2.44	**<0.001***
Sex N (%): • **Male**	15(60%)	11 (44%)	0.258
Positive consanguinity N (%):	11(44%)	10 (40%)	0.774

Analyzed by Kruskal-Wallis test, Mann-Whitney U test and Chisquare test
****: Significant difference at P value < 0.05***
Abbreviations : N: Number ; SD: Standard Deviation

Table 1 : Shows that the mean age of children with chronic ITP was significantly higher than that of newly diagnosed children where P value was <0.001.

Table 2: Comparison between studied groups regarding clinical data.

History	Newly diagnosed ITP (A) (N = 25)	Chronic ITP (B) (N = 25)	p value
Age of onset (years): • **Mean ± SD**	7.64 ± 1.97	8.12 ± 2.12	0.474
Bleeding manifestations N (%): • **Purpura & ecchymosis** • **Active bleeding** • **Both**	14(56%) 4(16%) 7(28%)	12(48%) 4(16%) 9(36%)	0.817

Severity of bleeding N (%): (Pediatric ITP Bleeding Scale) • **Mild** • **Moderate** • **Severe**	 14(56%) 11(44%) 0 (0%)	 12(48%) 13(52%) 0 (0%)	0.571
Treatment received (%): **Steroid** **Steroid & IVIG** **TPO-RAs (Eltrombopag)**	 7 (28%) 14 (56%) 4 (16%)	 0 (0%) 14 (56%) 11 (44%)	 **0.006***

-Analyzed by Chi square test
****: Significant difference at P value < 0.05***

Abbreviations :
N: Number ; SD: Standard Deviation ; IVIG: Intravenous Immunoglobulin ; TPO-RAs: Thrombopoietin Receptor Agonists

Table 2 : Shows that the chronic ITP children were significantly more frequent to use TPO agonist than newly diagnosed children where P value was 0.006.

Table 3: Comparison between studied groups regarding laboratory data.

	Newly diagnosed ITP (A) (N = 25)	**Chronic ITP (B) (N = 25)**	**P value**
Hemoglobin (g\dl): • **Mean ± SD**	 11.0 ± 0.80	 10.5 ± 0.87	 **0.043***
TLC (x10³\ml): • **Mean ± SD**	6.27 ± 1.27	6.16 ± 1.06	0.741
Platelet count (x10³\ml): • **Mean ± SD**	12.3 ± 5.72	28.1 ± 7.67	**<0.001***

Analyzed by Kruskal-Wallis test and Mann-Whitney U test
****: Significant difference at P value < 0.05***
Abrreviations : TLC :Total Leucocytic Count ; SD :Standard Deviation

Table 3 : Shows that the hemoglobin level was significantly higher in newly diagnosed ITP children than those with chronic ITP where P value was < 0.05.
As regarding platelets count, Newly diagnosed ITP children had significantly lower platelets count than children with chronic ITP where P value was < 0.05.

DISCUSSION

In the present study, The mean age of children with chronic ITP was significantly higher than that of those with newly diagnosed ITP (p<0.001). This observation aligns with several previous reports indicating that increasing age at diagnosis is associated with a higher likelihood of progression to chronic ITP **(9)**. **Adly et al., 2023** found statistical significance as patients with chronic ITP were older (p<0.001) and presented more frequently at age >5 years (p=0.027). But, **Mohamed et al., 2022** reported that the ages of newly diagnosed cases ranged between 1 to 13 years old with insignificant difference between them and chronic group **(10)**.

A significant difference was observed in the treatment modalities between studied groups where newly diagnosed patients most frequently received corticosteroids alone (28%) or in combination with IVIG (56%), reflecting initial management strategies aimed at rapid platelet recovery. Conversely, in chronic ITP, the predominant use of thrombopoietin receptor agonists (44%) underscores their established role as second-line therapy for persistent or refractory cases consistent with international consensus guidelines. Also, **Yosgat et al., 2020** provides evidence that thrombopoietin receptor agonists (Eltrombopag) is an effective and safe agent in the treatment of children with chronic or acute refractory ITP **(11)**. **Mohamed et al., 2022** showed that 78.9% received steroid therapy mainly oral therapy (57.9%). The same percentage 78.9% received IVIG therapy and about 73.7% received combined therapy. Only 2 patients received revolade, no one take immunosuppressive drugs and only 10.5% of patients had no medication and treated by observation only. **(10)**

In our study, Children with chronic ITP exhibited significantly lower hemoglobin levels compared to those with newly diagnosed ITP (p=0.043). This finding may reflect chronic or recurrent bleeding episodes, nutritional compromise and treatment-related anemia particularly in patients receiving prolonged corticosteroid therapy **(12)** or receiving thrombopoietin receptor agonists (Eltrombopag) as it is associated with development of iron deficiency anemia **(11)**. The platelet count was significantly higher in chronic ITP than in newly diagnosed cases where $p < 0.001$. but it still below the normal reference range. This pattern likely reflects partial platelet recovery or compensatory marrow response in chronic disease phases. On the contrary, **Erdogan et al., 2023** found that there was no significant difference between the acute ITP group and the chronic ITP group in laboratory findings **(14)**. Also, **Mohamed et al., 2022** showed no statistically significant correlation was found between laboratory findings and the course of the disease **(10).** As regarding total leucocytic count values, there was no significant difference between two groups ($p = 0.741$). Similar observations were reported by **Alpdogan et al., 2023** as there was no significant difference of TLC in both groups in their study and they were within normal ranges **(13)**.

Regarding bleeding manifestations, purpura and ecchymosis were the predominant findings in both groups, while active mucosal bleeding was less frequent. The distribution of bleeding types did not differ significantly ($p = 0.817$). According to the Pediatric ITP Bleeding Scale, most patients had mild-to-moderate bleeding and none exhibited severe bleeding in either group. This was in accordance with **Adly et al., 2023** who showed no significant difference was found as regards the site of bleeding except that patients with chronic ITP had higher incidence of epistaxis (p= 0.025). Also. this agrees with **Mohamed et al., 2022** who found that all cases presented by cutaneous bleeding, 47.4% of them presented with epistaxis and 57.9% of them presented by gingival hemorrhage, none of our patients developed intracranial hemorrhage (ICH) at diagnosis or during follow–up period. In constant, the results of **Makis et al., 2017** reported that in the newly diagnosed, 30 of 43 children (70%) had mucosal bleeding. Also, 2 patients presented with conjunctival hemorrhage and only one patient presented with menorrhagia **(15)**. This confirmed that ITP is frequently associated with cutaneous bleeding and rarely associated with life-threatening bleeding events at diagnosis **(9)**

We found that there was no statistically significant difference between the newly diagnosed and chronic ITP groups in terms of sex or consanguinity ($p = 0.258$ and $p = 0.774$ respectively). The majority of the studied cases were males (60%), while 40% of cases were females. This was in agreement with **Mohamed et al., 2022** who found male predominance in newly diagnosed ITP. On contrary to our results, **Makis *et al., 2017*** reported equal sex distribution among newly diagnosed cases **(15)**. In the present study males represented 60% of the newly diagnosed cases compared with 44% among chronic cases, consistent with the general pediatric pattern showing a slight male predominance at disease onset, which tends to balance or shift toward females with chronic disease. This finding supported by **Rosu et al., 2023** suggesting that chronic form is more frequent in older girls and considering that one of the main risk factors for chronicity **(16)**. Positive consanguinity was present in 44% of newly diagnosed patients and 40% of chronic ITP patients, without a significant difference ($p = 0.774$). Similarly, **Adly et al., 2023** found that there was no significant difference between newly diagnosed and chronic ITP as regards consanguinity (p=0.309)

The mean age of onset was slightly higher among children with chronic ITP compared with those newly diagnosed children, though the difference was not statistically significant ($p = 0.474$). This finding aligns with a study conducted by **Gungor et al., 2019** on a group of 209 children diagnosed with ITP, the average age at the onset of the chronic form was 6.8 years compared to the average age at the onset of the acute form of the disease of 4.8 years **(17)**. Several previous studies indicating that being over 10 years old at diagnosis have been reported as a risk factor for chronicity even if not reaching statistical significance **(16)**.

CONCLUSION

Our study concluded that the mean age of children with chronic ITP was significantly higher than that of those with newly diagnosed ITP. Therapeutic patterns differed significantly, with corticosteroids and IVIG being the mainstay in newly diagnosed cases, while thrombopoietin receptor agonists were predominantly used in chronic disease. Chronic ITP patients had significantly lower hemoglobin levels, while platelet counts were higher. Study groups presented mainly with cutaneous bleeding but severe hemorrhagic events were absent.

Limitations of study

Limitations of this study were the relatively small sample size and single-center design.

Abbreviations

ITP	Immune Thrombocytopenia
CBC	Complete Blood Count
TPO-RAs	Thrombopoietin Receptor Agonist
TLC	Total Leucocytic Count
ASH	American Society of Hematology
IVIG	Intravenous Immunoglobulin
IBLS	ITP Bleeding Scale
Hb	Hemoglobin
SD	Standard Deviation
N	Number
ICH	Intracranial Hemorrhage

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Author Contributions:

- **Zamzam Hassan Mohamed:** Contribute methodology, statistical analysis, write manual script and supervision of clinical work.
- **Suzan Omar Mousa :** Methodology design, data interpretation, and supervision of clinical work.
- **Samir Tamer Abd-Allah:** Conceptualization, supervision, and critical revision of the manuscript for important intellectual content.
- **Hind Mohamed Moness Ali:** Laboratory work supervision and data analysis support.
- **Sara Gamal Hares Motawea:** Data collection, laboratory analysis, statistical processing, drafting of the manuscript, and corresponding author responsibilities.
- **Asmaa Hosni Abdel Hafez:** Analysis of data and help in writing manual script.

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