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RECENTLY DISCOVERED IMMUNE THROMBOCYTOPENIA IN CHILDREN – AN ANALYTICAL STUDY

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ABSTRACT

Background: Evaluating immune thrombocytopenia (ITP) outcomes is critical in the Indian setting in order to get insight into the laboratory, clinical, and pathological variables that are associated with a higher risk of chronicity or illness persistence.

Aim: The purpose of this study was to evaluate the predictors and results of paediatric patients with recently diagnosed immune thrombocytopenia.

Methods: The study evaluated paediatric patients with newly diagnosed thrombocytopenia, ages ranging from 1 month to 18 years. Along with illness predictors and outcomes, laboratory, clinical, and pathological variables were evaluated in all included patients.

Results: Three participants were followed for three to twelve months, whereas 29 subjects had a minimum follow-up of one year. Study participants had an average age of 8.2±3.4 years, with 62.5% (n=20) being female. There was intracranial bleeding in 62.5% (n=10) and wet bleeding in 56.25% (n=18) of the individuals, respectively. There were 41.4% (n=12/29) and 65.6% (n=21/32) of participants with chronic and persistent ITP, respectively. At a year, ALC was 2.96 x103/µL and 3.99 x103/µL, respectively, in participants who had no reaction and those who had an overall response (p=0.03). The treated group had a nearly 10% lower reaction than the non-treated group.

Conclusion: The current investigation comes to the conclusion that there is a larger incidence of cerebral haemorrhage and chronicity than what has been documented in the literature. In individuals with thrombocytopenia, the response is correlated with higher absolute leucocyte counts.

Keywords: ITP, platelet, morbidity, persistent ITP, thrombocytopenia

INTRODUCTION

Immunothrombocytopenia, or ITP, is a clinical disease that is most frequently caused by acquired thrombocytopenia in juvenile individuals. It is thought that immune thrombocytopenia is a benign condition that does not cause the afflicted kid subjects to bleed excessively. In the very unusual event if the afflicted kid subjects have immunological thrombocytopenia, there may be severe bleeding as well as high rates of morbidity and death.1, 2

The children with immunological thrombocytopenia have a considerably lower quality of life since they are typically unable to carry out their everyday activities without being traumatised, which can lead to more severe bleeding. Generally speaking, immune thrombocytopenia is a self-limiting illness.

However, it may result in chronic or persistent immunological thrombocytopenia in around 25–30% of the afflicted children. There is still a lack of clarity in the research on the risk variables that are linked to severe bleeding and chronicity or persistence. The majority of the literature now in existence that evaluates the prognosis in paediatric patients with immune thrombocytopenia comes from Western nations, with very little data coming from developing countries like India.3,4

Therefore, in order to get a foundational understanding of the laboratory, clinical, and pathological findings that predispose to the chronicity or persistence of the disease, it is imperative that the outcomes of immunological thrombocytopenia in Indian individuals be thoroughly assessed and studied.5. The purpose of the current study was to evaluate the kid patients who had acquired persistent or chronic immune thrombocytopenia and had just received a diagnosis of immune thrombocytopenia. Assessing the risk variables linked to the emergence of persistent or chronic immunological thrombocytopenia was another goal of the investigation.

MATERIALS AND METHODS

The current clinical investigation, which is both retrospective and prospective (mixed), aims to evaluate the predictors and outcomes of children with recently diagnosed immune thrombocytopenia. The purpose of this study was to evaluate children with newly diagnosed immune thrombocytopenia who went on to develop chronic or persistent immune thrombocytopenia. Assessing the risk variables linked to the emergence of persistent or chronic immunological thrombocytopenia was another goal of the investigation. The research participants originated from the Institute's Paediatric Department. Before each participant participated in the study, their parents gave their verbal and written informed consent.

Following a clinical assessment, child subjects with platelet counts <100x103/µL and normal peripheral smear examination results were diagnosed with immune thrombocytopenia, with the exception of thrombocytopenia, which was defined as the absence of any abnormal phenotype findings, such as absent radius and Fanconi anaemia features, fever, joint pain, significant lymphadenopathy, and any organomegaly. When marrow failure syndrome or congenital thrombocytopenias were suspected, or if the individual was a baby, a bone marrow examination was performed as a preliminary evaluation. Clinical information was evaluated for each individual, including presenting complaints, examination results, follow-up information, and therapy specifics. Immunomodulatory medication was often not administered to child participants with immunological thrombocytopenia when they showed signs of dry bleeding without a platelet count.

Immunomodulatory medication was given to child participants who experienced wet bleeding at any point throughout the trial or who declined observatory treatment; the decision to administer immunomodulatory treatment was left up to the treating paediatric haematologist. In the paediatric haematology clinic, child participants were seen monthly for the first three months, and then every three months for the remaining twelve months. Clinical information was obtained for participants evaluated retroactively from the institute's prior records. To determine the results, the platelet counts were measured three and twelve months after the diagnosis. The 2009 International Working Group definition for immune thrombocytopenia in children and adults was used to establish the outcomes/disease phase and response criteria in cases with newly diagnosed, persistent, and chronic immune thrombocytopenia.6

Newly diagnosed immune thrombocytopenia was defined as from diagnosis time to 3 months from diagnosis. A diagnosis of persistent immune thrombocytopenia was made if the patient's platelet counts were less than 100x103/µL, and the condition persisted for three to twelve months after treatment without spontaneous remission or full therapeutic response. ITP lasting more than 12 months was classified as chronic immune thrombocytopenia. A complete response was defined as no bleeding and a platelet count of at least 100x109/L. Platelet counts between 30 and 100 x109/L, a minimum 2-fold rise in the baseline platelet count, and the absence of bleeding were considered partial responses. The treatment was discontinued when the platelet count was less than 30x109/L. A platelet count of less than 30x109/L, a platelet count that increased by less than two times from the baseline value, or clinical bleeding following partial or total remission were considered losses in response.

If the patient's platelet counts were fewer than 100x103/µL and the disease remained for three to twelve months following therapy without a full therapeutic response or spontaneous remission, it was diagnosed as chronic immune thrombocytopenia. When ITP persisted for more than a year, it was labelled as chronic immune thrombocytopenia. Complete response was characterised by at least 100x109/L of platelets and no haemorrhage. Partial responses were

defined as platelet counts between 30 and 100 x109/L, a minimum 2-fold increase in baseline platelet count, and no bleeding. When the platelet count was less than 30x109/L, the therapy was stopped. Losses in response were defined as platelet counts of less than 30x109/L, counts that rose by less than two times from the baseline value, or clinical bleeding after either partial or complete remission.

For the purpose of evaluating descriptive measures, the collected data were statistically analysed using SPSS (Statistical Package for the Social Sciences) software version 16.0 (SPSS Inc., Chicago, USA). The findings were presented as percentages, frequency, mean, and standard deviation. When the p-value was less than 0.05, it was deemed statistically significant. The Chi-square test was used to determine the research parameters' significance on the categorial scale.

RESULTS

The current clinical investigation, which is both retrospective and prospective (mixed), aims to evaluate the predictors and outcomes of children with recently diagnosed immune thrombocytopenia. 29 participants had a minimum follow-up of one year, while three subjects had follow-ups ranging from three to twelve months. Study participants had an average age of 8.2±3.4 years, with 62.5% (n=20) being female.

When the features of the study patients (n=32) were assessed at three months for the development of chronic and persistent ITP, from full remission and persistent ITP, 37.5% (n=6) and 62.5% (n=10) individuals were not treated, demonstrating statistical non-significance with p=0.77. Fever history was seen in 28.57% (n=4) of participants with chronic ITP and 62.5% (n=10) of subjects with persistent ITP, respectively (p=0.94). Table 1 demonstrates that there were statistically non-significant differences in wet bleeding, symptom duration, female gender, and age ≤10 years between the chronic and persistent ITP groups (p=0.85, 1.00, 0.61, and 0.23, respectively).

After evaluating the relationship between the development of chronic and persistent ITP in the study participants (n = 29) at a 12-month follow-up, it was observed that 60% (n = 9) and 40% (n = 6) of the individuals did not get treatment leading to full remission, with the persistent ITP groups exhibiting statistical non-significance at p = 0.43.

Complete remission and persistent ITP showed no relationship to fever history, with 66.6% (n = 8) and 33.3% (n = 4) of the individuals showing statistical non-significance with p = 0.44, respectively. Wet bleeding was observed in 62.5% (n = 10) of participants with full remission and 37.5% (n = 6) of persons with chronic ITP, respectively (p = 0.26). A statistical non-significance was seen in the full remission and chronic ITP groups for symptom durations less than 14 weeks (p=0.65). Table 2 shows that age ≤10 years and female gender also had a non-significant influence on the full remission and persistent ITP groups, with p=1.00 and 0.87, respectively.

There were 41.4% (n=12/29) and 65.6% (n=21/32) of participants with chronic and persistent ITP, respectively. Of the 17 participants that exhibited a full reaction after 12 months, 58.8% (n = 10) showed a complete response at 3 months, and 41.1% (n = 7) showed a complete response during the next 9 months.

High ALC (absolute lymphocyte counts) at admission was linked to an overall partial or full response at 3 and 12 months. The median ALC at admission for participants with overall and no response was 2.87 x103/µL with p=0.02, and 3.77 x103/µL. At a year, ALC was 2.96 x103/µL and 3.99 x103/µL, respectively, in participants who had no reaction and those who had an overall response (p=0.03). The treated group had a nearly 10% lower reaction than the non-treated group.

It was observed that no immunomodulatory treatment of any kind was administered to 50% of the participants. For 14 days, 12.5% (n=4) of the individuals received oral prednisolone at a dose of 1 mg/kg. Intravenous immunoglobulin (IVIG) at a dosage of 1 g/kg administered alone, and methylprednisolone (MP) at a dose of 30 mg/kg administered alone for three days in 15.6% (n=5) High ALC (absolute lymphocyte counts) at admission was linked to an overall partial or full response at 3 and 12 months. The median ALC at admission for participants with overall and no response was 2.87 x103/µL with p=0.02, and 3.77 x103/µL. At a year, ALC was 2.96 x103/µL and 3.99 x103/µL, respectively, in participants who had no reaction and those who had an overall response (p=0.03). The treated group had a nearly 10% lower reaction than the non-treated group.

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Overall, no significant difference was seen in the 18 participants without a history of fever, and 33.3% (n = 6) and 66.6% (n = 12) of the subjects, respectively, had no reaction (p = 0.94). Of the eighteen participants who had wet bleeding, 38.8% (n=7) and 61.1% (n=11) showed no reaction overall; this difference was statistically not significant (p=0.85). Table 3 summarises that for female gender and age ≤10 years, there was a statistically non-significant difference (p=0.61 and 0.23, respectively) and no response.

In terms of the relationship between clinical variables and the overall response at 12 months in study participants—of which 15 were not treated—it was seen that full remission and persistence were observed in 80% (n=12) and 20% (n=3) of study participants, respectively, and that these findings were statistically non-significant (p=0.12).

Full remission and persistence were observed in 68.75% (n=11) and 31.25% (n=5) of the 16 participants who had no prior history of fever, respectively, with p=0.44. Complete remission and chronic ITP were observed in 69.23% (n=18) and 30.76% (n=8) of the 26 participants with symptoms lasting less than 14 days, respectively. These findings were non-significant, with p=1.00. Table 4 displays a non-significant difference between p=0.33 and 1.00 for full remission and chronic ITP, respectively, based on female gender and age ≤10 years.

DISCUSSION

29 participants had a minimum follow-up of one year, while three subjects had follow-ups ranging from three to twelve months. Study participants had an average age of 8.2±3.4 years, with 62.5% (n=20) being female.

After evaluating the relationship between the development of chronic and persistent ITP in the study participants (n=32) after three months, it was observed that 37.5% (n=6) and 62.5% (n=10) of the individuals with persistent ITP and complete remission were not treated, demonstrating statistical non-significance with p=0.77. Fever history was seen in 28.57% (n=4) and 62.5% (n=10) of the participants with persistent and chronic ITP, respectively (p=0.94). In the chronic and persistent ITP groups, wet bleeding, duration of symptoms, female gender, and age ≤10 years revealed statistically non-significant differences (p=0.85, 1.00, 0.61, and 0.23, respectively). These results were comparable to those of studies conducted in 2011 by Neunert C et al7 and in 2022 by Provan D8 in which the authors evaluated patients with thrombocytopenia and traits comparable to those of the current investigation.

When examining the relationship between study participants (n=29) and the development of chronic and persistent ITP at a 12-month follow-up, it was shown that 60% (n=9) and 40% (n=6) of the individuals did not get treatment leading to full remission, with persistent ITP groups displaying statistical non-significance at p=0.43. Fever history had no influence on either full remission or persistent ITP, with statistical non-significance (p=0.44) shown in 66.6% (n=8) and 33.3% (n=4) of the individuals, respectively. Of the participants with full remission and chronic ITP, wet bleeding was observed in 62.5% (n = 10) and 37.5% (n = 6), respectively (p = 0.26). A statistical non-significance was seen in the full remission and chronic ITP groups for symptom durations less than 14 weeks (p=0.65). For the full remission and persistent ITP groups, age ≤10 years and female gender exhibited non-significant effects, with p=1.00 and 0.87, respectively.

The findings aligned with the research conducted by Bao W et al9 in 2010 and Ahmed I10 in 2010, wherein the authors documented a correlation between the development of chronic and persistent ITP and comparable features in their study participants.

There were 41.4% (n=12/29) and 65.6% (n=21/32) of participants with chronic and persistent ITP, respectively. Of the 17 participants that exhibited a full response after 12 months, 58.8% (n=10) of them showed it at 3 months, and 41.1% (n=7) of them showed it during the next 9 months. High ALC (absolute lymphocyte counts) at admission was linked to an overall partial or full response at 3 and 12 months. The median ALC at admission for participants with overall and no response was 2.87 x103/µL with p=0.02, and 3.77 x103/µL.

At a year, ALC was 2.96 x103/µL and 3.99 x103/µL, respectively, in participants who had no reaction and those who had an overall response (p=0.03). The treated group had a nearly 10% lower reaction than the non-treated group. These results were consistent with those of studies conducted in 2013 by Rodeghiero F et al. and in 2010 by Bansal D et al., who reported comparable complete and no response in their participants after receiving therapy for thrombocytopenia. According to the study's findings, 50% of the participants received no immunomodulatory treatment at all. For 14 days, 12.5% (n=4) of the individuals received oral prednisolone at a dose of 1 mg/kg.

The patients received IVIG (intravenous immunoglobulin) as a single dose of 1 gm/kg, MP (methylprednisolone) as a single dose of 30 mg/kg for three days in 15.6% (n=5) of the patients, MP and IVIG combined in 6.25% (n=2) of the

patients, and prednisolone combined with either dapsone and in 9.4% (n=3) or with azathioprine in 6.25% (n=2) of the patients, respectively. The secondary aetiology of kid individuals with chronic immunological thrombocytopenia was assessed. The immunoglobulin profiles of all the kid participants were normal, and their hepatitis B and C virus tests came back negative. Two of the juvenile participants had positive ANA results, while every subject had negative ENA blot results. Four research participants had their symptoms of hypothyroidism evaluated. These outcomes were consistent with research conducted by Koçak U et al13 in 2007 and Grace RF et al[14] in 2012 where treatment therapy similar to the present study was also utilized by the authors in their studies for subjects with thalassemia.

Regarding the relationship between clinical variables and overall response after three months in research participants, it was observed that, of the sixteen people who were not treated, 37.5% (n = 6) and 62.5% (n = 10) of study participants showed overall and no response, respectively, demonstrating statistical non-significance with p=0.77. Overall, no significant difference was seen in the 18 participants without a history of fever, and 33.3% (n = 6) and 66.6% (n = 12) of the subjects, respectively, had no reaction (p=0.94). Of the eighteen participants who had wet bleeding, 38.8% (n=7) and 61.1% (n=11) showed no reaction overall; this difference was statistically not significant (p=0.85). For female gender and age ≤10 years, there was a comparable statistically non-significant difference and no response (p=0.61 and 0.23, respectively).

These results were in line with those of Diab AM et al. (15 in 2021) and Güngör T et al. (16 in 2019), whose conclusions about the relationship between clinical variables and overall response were consistent with the findings of the current investigation.

According to the study's findings, complete remission and persistence were observed in 80% (n=12) and 20% (n=3) of the study subjects, respectively, with p=0.12 indicating statistical non-significance for the relationship between clinical factors and overall response at 12 months in the study subjects, targeting 15 subjects who were not treated. Full remission and persistence were observed in 68.75% (n=11) and 31.25% (n=5) of the 16 participants who had no prior history of fever, respectively, with p=0.44.

Complete remission and chronic ITP were observed in 69.23% (n=18) and 30.76% (n=8) of the 26 participants with symptoms lasting less than 14 days, respectively. These findings were non-significant, with p=1.00. A comparable non-significant difference (p=0.33 and 1.00) was seen for full remission and chronic ITP in females aged ≤10 years and older. The results were consistent with the findings of Zeller B et al. (2017) and Psaila B et al. (2018), which showed comparable associations between clinical variables and overall response at one year in their respective investigations.

CONCLUSION

The current investigation comes to the conclusion that the incidence of chronicity and cerebral haemorrhage are greater than those found in published literature. Increased absolute leucocyte counts are linked to a response in thrombocytopenia patients. For more accurate results, longer-term research in the future is necessary.

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TABLES

Characteristics	Complete remission		Persistent ITP		p-value
	n	%	n	%	
Not treated (n=16)	6	37.5	10	62.5	0.77
Fever history (n=14)	4	28.57	10	62.5	0.94
Wet bleeding (18)	7	38.8	11	61.1	0.85
Symptom duration <14 days (n=28)	9	32.14	19	67.85	1.00
Female gender (n=20)	7	35	13	65	0.61
Age ≤10 years (23)	6	26.08	17	73.91	0.23

Table 1: Association of characteristics and development of chronic and persistent ITP in study subjects (n=32) at 3 months

Characteristics	Complete remission		Persistent ITP		p-value
	n	%	n	%	
Not treated (n=15)	9	60	6	40	0.43
Fever history (n=12)	8	66.6	4	33.3	0.44
Wet bleeding (16)	10	62.5	6	37.5	0.26
Symptom duration <14 days (n=26)	16	61.53	10	38.46	0.65
Female gender (n=18)	10	55.5	8	44.4	1.00
Age ≤10 years (22)	13	59.09	9	40.90	0.87

Table 2: Association of characteristics and development of chronic and persistent ITP in study subjects (n=29) at 12 months

Clinical parameter	Overall response		No response		p-value
	n	%	n	%	
Not treated (n=16)	6	37.5	10	62.5	0.77
Fever history absent (n=18)	6	33.3	12	66.6	0.94
Wet bleeding (18)	7	38.8	11	61.1	0.85
Symptom duration <14 days (n=28)	9	32.14	19	67.85	1.00
Female gender (n=20)	7	35	13	65	0.61
Age ≤10 years (23)	6	26.08	17	73.91	0.23

Table 3: Association of clinical factors to overall response at 3 months in study subjects

Characteristics	Complete remission		Persistent ITP		p-value
	n	%	n	%	
Not treated (n=15)	12	80	3	20	0.12
Fever history absent (n=16)	11	68.75	5	31.25	0.82
Wet bleeding (16)	12	75	4	25	0.44
Symptom duration <14 days (n=26)	18	69.23	8	30.76	1.00
Female gender (n=18)	13	72.22	5	27.77	0.33
Age ≤10 years (22)	15	68.18	7	31.81	1.00

Table 4: Association of clinical factors to overall response at 12 months in study subjects