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# Predictive and Prognostic Value of Mean Platelets Volume in Immune Thrombocytopenia in Children: Review Article

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## ABSTRACT

**Background:** Platelet counts (PLT) of less than 100 x $10^9$/L are diagnostic of immune thrombocytopenia (ITP), a kind of acquired thrombocytopenia. High rates of destruction of platelets and decreased platelet synthesis are the root causes of thrombocytopenia among cases with primary immune thrombocytopenia. ITP cannot be definitively diagnosed; consequently, primary ITP is still a diagnosis of exclusion made after all other possible etiologies of thrombocytopenia have been ruled out. Multiple studies have found elevated mean platelet volume (MPV) levels in patients with ITP, raising the prospect of using MPV as a diagnostic and prognostic marker for the disease. However, there has not been sufficient research into the clinical significance of MPV in children with ITP.

**Objective:** This review article aimed to assess the role mean platelet volume in the diagnosis and prognosis of ITP.

**Methods:** Mean platelet volume, pediatrics, and idiopathic thrombocytopenia were all looked for in PubMed, Google scholar, and Science direct. References from relevant literature were also evaluated by the authors, but only the most recent or complete studies from January 2000 to May 2021 were included. Due to the lack of sources for translation, documents in languages other than English have been ruled out. Papers that did not fall under the purview of major scientific investigations, such as unpublished manuscripts, oral presentations, conference abstracts, and dissertations, were omitted.

**Conclusion:** It is possible to predict the course of ITP in children by monitoring changes in mean platelet volume (MPV) throughout time and the MPV at diagnosis.

**Keywords:** Mean platelet volume, Idiopathic thrombocytopenia, Pediatric.

## INTRODUCTION

Reduced platelet count in the peripheral blood is a hallmark of the autoimmune disorder known as immune thrombocytopenia, which is caused by antibodies directed against platelet surface antigens and reticuloendothelial system macrophages resulting in destruction of platelets and thrombopoiesis abnormalities **(1)**.

The estimated annual incidence among American kids ranges from 1 to 6.4 per 100,000. Due to the fact that reported instances are based on symptomatic ITP requiring hospitalization rather than total ITP cases, researchers estimate the annual incidence in children is likely greater. Although it can occur at any time in a child's life, the most common ages are between 2 and 5 years old, with another peak in puberty. There is a small gender gap between infants and young children, with boys slightly outmatched girls **(2)**.

As the smallest of the blood's morphotic components, thrombocytes are also among the most reactive. First and foremost, they contribute to fibrosis and normal hemostasis. It has been shown to serve several purposes, as recent research has shown. Platelets are the first blood cells to arrive at an injury site and undergo dramatic morphological changes in response to classical agonists such as adenosine diphosphate (ADP), a specific thromboxane (TX) A2 receptor antagonist (TXA2), a platelet-activating factor (PAF) antagonist, and inflammatory cytokines (TNF alpha, IL-6, and IL-1). As a result, they promote inflammation and fibrosis **(3)**.

Hematological analyzers used the volume distribution of blood cells for evaluation of mean platelet volume (MPV) and precise assessment of their size. The normal platelet mean granularity ranges from 7.5 to 12.0 fl, and the proportion of big platelets should be between 0.2 and 5.0%. Maintaining hemostasis and a steady platelet mass is linked to an inverse relationship between MPV and platelet count under normal settings **(4)**.



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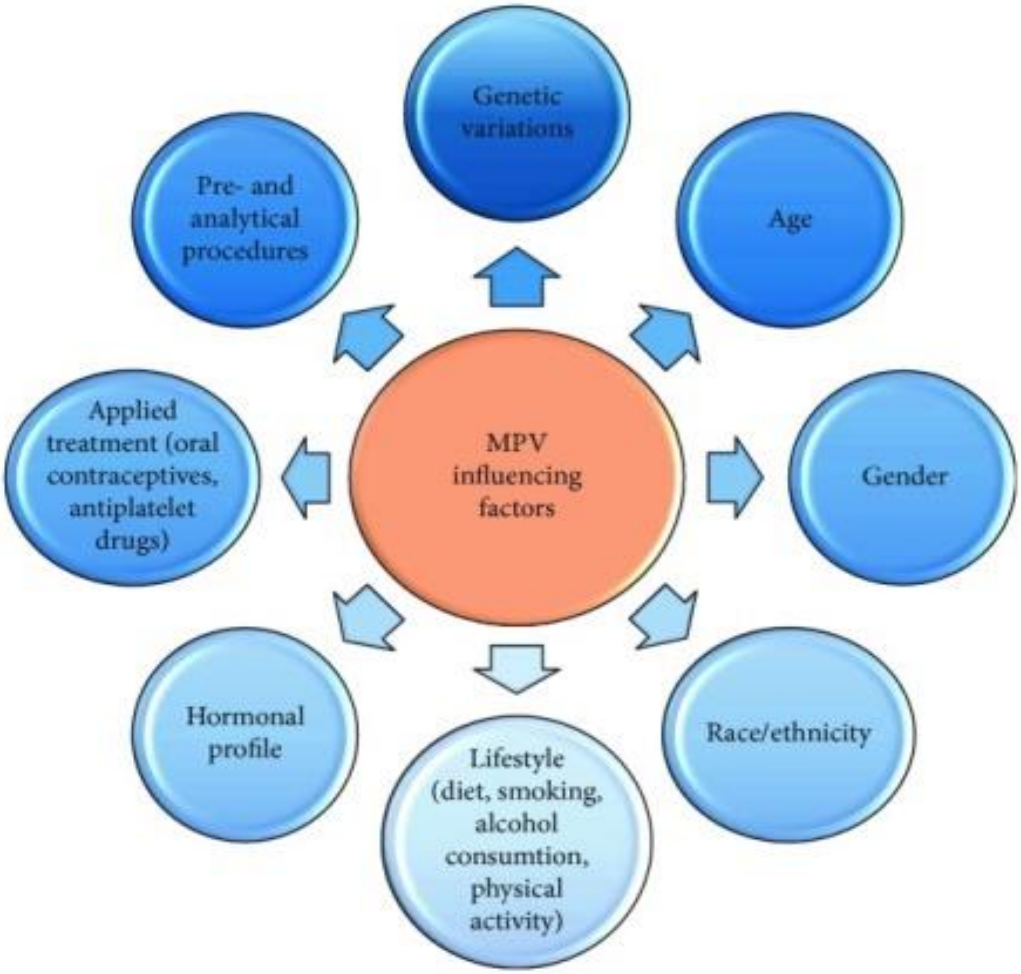


**Figure (1):** Mean platelet volume influence factors [(4)].

Because of this, these characteristics have been proposed for use in the diagnosis of a variety of illnesses. More importantly, MPV is a measure of platelet activity because of its correlation with platelet activity. There is a wide variety of platelets in the blood. Higher MPV (>15 fl) carriers tend to be younger and more reactive than those with normal MPV [(3)].

**DIAGNOSTIC ROLE OF MPV IN ITP PATIENTS**

Patients with ITP have normal or slightly elevated mean platelet volumes, but nearly all patients with hereditary thrombocytopenia have abnormal platelet volumes (marco- or micro-thrombocythemia). For example, in cases with hereditary thrombocytopenia, where platelet volume may be 50–100% greater than normal due to a lack of established criteria, this test becomes crucial. Inherited thrombocytopenia (IT) is characterized by this criterion, which is said to be beneficial in separating IT from immune thrombocytopenia due to abnormalities in platelet size [(5)].

Platelet macrocytosis is a feature of many types of IT, hence measuring platelet size is well recognised as a useful method of raising suspicion of this group of diseases. MYH9-related disease (MYH9-RD), monoallelic and biallelic Bernard-Soulier syndrome (BSS), and other less prevalent forms of IT can present platelets that, due to their high size, are difficult for the body to handle and are not identified by electronic counters, resulting in an underestimate of the patient's platelet count and mean platelet volume [(6)]. This makes it difficult to compare MPV readings acquired at multiple facilities since different instruments measure MPV in healthy individuals or those with non-macrocytic thrombocytopenia in different ways. **Noris and colleagues** [(6)] found that the utility of platelet size evaluation in differentiating between ITP and inherited macr-othrombocytopenias has been shown as the MPV values produced by appropriate cell counters. If the counter's platelet count does not match a manual count, or if peripheral blood films show excessively large platelets in persons with normal or slightly elevated MPV, inaccuracies can be detected concerning this way[(6)].

We propose combining microscopy analysis of blood films with cell counter measurements of MPV. Examination of a blood film makes the diagnosis of inherited macro-thrombocytopenia likely. Increased mean platelet volume (MPV) of more than 51% compared to controls is a strong indicator of a hereditary macro-thrombocytopenia if very large platelets are not detected [(6)].

Automated blood analyzers now under development have several parameters that can be utilised to diagnose thrombocytopenia's underlying causes. Due to its ubiquitous availability, MPV is one of the automated platelet metrics that has been studied extensively in the context of this goal. Prior research indicated that patients experiencing bone marrow (BM) hypoplasia or thrombocytopenia as a result of cytotoxic medicines or chemotherapy had a low MPV **(7).**

ITP patients had higher MPV and PDW levels than healthy people overall, but the differences between ITP and aplastic anemia were more pronounced. Individuals with ITP reported increased MPV and PDW when compared to those with hypoproductive thrombocytopenia. Immune-mediated peripheral injury triggers a compensatory thrombopoiesis in the bone marrow, which may explain why patients with ITP have higher MPV values than healthy individuals **(8).**

## PROGNOSTIC ROLE OF MPV IN ITP PATIENTS

**Ahmed *et al.*** **(9)** discovered that the presence of reported MPV was an independent predictive predictor for achieving a long-lasting CR in paediatric ITP. These data confirmed the efficacy of MPV as a predictor factor for chronic ITP in children, but they used linear extrapolation or didn't take important possible factors into consideration**.** Moreover, **Chen *et al.*** **(10)** reported that a comparison was made between the findings obtained using MPV as a categorical variable (quartiles) and the p-value for trend. Results were found to be positive. To further understand the non-linear association between MPV and ITP relapse, researchers used the generalized additive model (GAM). GAM's greatest strength is its ability to manage relationships that are not linear **(11).**

Non-parametric smoothing can be accommodated in this model, and the data can be fitted with a regression spline. Greater insight into the relationship between treatment and outcome can be gained by using GAM **(12),** than 8 fl revealed slightly greater risks of acute ITP diagnosis, although the difference was not statistically significant. The sample size of our research is probably too small to provide a statistically significant answer to the MPV prediction or to any treatment-related parameters **(13).**

## MPV AFTER ITP TREATMENT

**Omar *et al.*** indicated that the primary goal of treatment for patients with a new diagnosis is to quickly achieve a safe platelet count (>20 - 30 $10^9$/l) in order to avoid or stop haemorrhages and to guarantee an adequate quality of life with minimum treatment-related harm. For the treatment of primary ITP, corticosteroids are typically used. When corticosteroids are taken alone, between 65% and 70% of patients improve after receiving an oral dose of 0.5 to 2 mg/kg daily. High response rate (full response + partial response) to initial treatment was achieved in 42 (84%) of patients in our study, while 8 (16%) patients did not **(13).**

Post-treatment platelet counts increased in both study groups, and MPV levels dropped. The majority of the patients in our study responded to the initial treatment, which may explain the reduction in values seen afterward. Results for platelet distribution width (PDW) values at presentation and after therapy were comparable between the two groups **(14).** Results like these are in accordance with those observed by **Korkmaz and coworkers** **(15)** who found that MPV was elevated in individuals with ITP but returned to normal following initial treatment. A possible mechanism by which steroid treatment enhances platelet survival without also improving platelet generation (platelet turnover) is the suppression of antibody production and the impairment of RES phagocytic activity. After starting steroids, both children and adults experience an increase in mature, small platelets and a decrease in activated, large platelets **(14).**

**Korkmaz *et al.*** (15) reported that the patient's PCT levels increased. PLT count and PCT steadily increased once therapy began, whereas PDW and MPV decreased. While, MPV was positively associated with PDW, it was inversely related to PLT count. The findings of these investigations are in agreement with those of **Fan and Wei** **(16)** who found that adjusting platelet parameters improved the accuracy of diagnosis and the understanding of treatment outcomes for patients with ITP (13)**.**

## MULTIAGENT THERAPY

### Dexamethasone and Rituximab:

Response rates at 6 and 12 months are improved in individuals with ITP who receive both rituximab and high-dose dexamethasone. Longer follow-up is needed to see if combination therapy cures more patients than either medication alone or only delays relapse in those patients, which in turn affect the MPV **(17)**.

For a total of 21 patients, researchers in Mexico utilized a single treatment: four weeks of weekly high-dose dexamethasone and low-dose rituximab (100 mg) therapy. If the platelet count decreased below 20 $10^9$/l by day 30, a second high-dose dexamethasone cycle was approved. At the end of six months, 16 patients (76%) achieved a complete response (platelet count of 100 $10^9$/L). 84% of patients had no recurrence (platelet count 30 $10^9$/L) at 12 months **(18).**

### Dexamethasone and thrombopoietin receptor agonist:

In a single-arm study, dexamethasone and eltrombopag were both employed. Newly diagnosed ITP was treated with dexamethasone 40 mg daily on days 1–4 and eltrombopag 50 mg daily on days 5–32 in a single cycle for 12 Mexicans. Nine patients had a persistent response (platelet count of 30 109/l after six months) and eight patients had a persistent response after 12 months, which is in accordance with previous studies' findings. An expanded and more controlled investigations are required to verify these preliminary findings, which

could also modify MPV, which could monitor prognosis [18].

## CONCLUSION

It is possible to predict the course of ITP in children by monitoring changes in mean platelet volume (MPV) throughout time and the MPV at diagnosis.

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**Author contribution:** Authors contributed equally in the study.

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