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CLINICAL PROTOCOL FOR DIAGNOSIS AND TREATMENT OF IMMUNE THROMBOCYTOPENIA DURING PREGNANCY

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Abstract. Immune thrombocytopenia (ITP) during pregnancy presents significant diagnostic and therapeutic challenges due to the potential risks to both mother and fetus. This study aimed to develop and validate a clinical protocol for the diagnosis and management of ITP in pregnant patients. A total of 62 pregnant women with confirmed ITP were treated according to a stepwise protocol involving initial corticosteroid therapy, intravenous immunoglobulin (IVIG) for corticosteroid-resistant or contraindicated cases, and second-line agents for refractory patients. Diagnostic workup excluded other causes of thrombocytopenia, ensuring accurate diagnosis. The protocol demonstrated high efficacy with favorable maternal and neonatal outcomes, including minimal bleeding complications and safe delivery conditions. Corticosteroids and IVIG were generally well tolerated, though careful monitoring for adverse effects was necessary. This protocol provides a practical, evidence-based framework for managing ITP during pregnancy, improving treatment outcomes and patient safety. Further studies are recommended to optimize therapy and long-term follow-up.

Keywords: Immune thrombocytopenia, pregnancy, clinical protocol, corticosteroids, intravenous immunoglobulin, diagnosis, treatment, maternal outcomes, neonatal outcomes, refractory ITP

Introduction

Immune thrombocytopenia (ITP) during pregnancy represents a significant clinical challenge due to its potential adverse effects on both maternal and fetal health. ITP is an autoimmune disorder characterized by isolated thrombocytopenia, defined as a platelet count below 100 × 10^9/L, resulting from increased platelet destruction and impaired platelet

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production caused by autoantibodies directed against platelet antigens. In pregnancy, the diagnosis and management of ITP require careful differentiation from other causes of thrombocytopenia, such as gestational thrombocytopenia, preeclampsia, HELLP syndrome, and other hematologic or systemic disorders. The physiological changes of pregnancy, including hemodilution and increased platelet turnover, further complicate diagnosis and treatment decisions.

The clinical importance of immune thrombocytopenia during pregnancy lies in the risk it poses to both the mother and fetus. For the mother, severe thrombocytopenia increases the risk of bleeding complications during pregnancy, labor, and delivery, which can lead to maternal morbidity and mortality if not managed appropriately. For the fetus and neonate, there is a risk of thrombocytopenia secondary to transplacental passage of maternal antiplatelet antibodies, which may result in bleeding complications such as intracranial hemorrhage. Hence, the primary goal of management in pregnant patients with ITP is to maintain a safe platelet count that minimizes bleeding risk while avoiding unnecessary interventions that may endanger the fetus.

Currently, clinical protocols for diagnosing and treating ITP during pregnancy vary widely, reflecting a lack of universally accepted guidelines. The diagnostic approach typically begins with thorough clinical evaluation, exclusion of other causes of thrombocytopenia, and laboratory investigations, including platelet counts, peripheral blood smear examination, and tests for autoimmune markers. Bone marrow examination is rarely required unless other hematologic conditions are suspected. Treatment strategies must be individualized based on the severity of thrombocytopenia, bleeding risk, gestational age, and response to therapy.

First-line treatment usually involves corticosteroids or intravenous immunoglobulin (IVIG), both of which are considered relatively safe during pregnancy. Corticosteroids act by suppressing the immune response and reducing platelet destruction, while IVIG interferes with Fc receptor-mediated platelet clearance. However, long-term corticosteroid use is associated with maternal complications such as gestational diabetes, hypertension, and increased risk of infections. IVIG, while effective, is costly and may require repeated administrations. Other second-line therapies, such as rituximab, thrombopoietin receptor agonists, and splenectomy, have limited data regarding safety in pregnancy and are generally reserved for refractory cases.

The development of a clinical protocol that standardizes the diagnosis and management of immune thrombocytopenia in pregnancy is crucial to optimize maternal and fetal outcomes. Such a protocol should include clear diagnostic criteria, risk stratification, treatment algorithms, and recommendations for monitoring during pregnancy, delivery, and the postpartum period. Furthermore, interdisciplinary collaboration among obstetricians, hematologists, and neonatologists is essential to provide comprehensive care.

In addition to clinical management, counseling patients about the disease, its potential complications, and treatment options is vital to ensure informed decision-making and adherence to therapy. Monitoring should also extend beyond delivery, as postpartum flare-ups of thrombocytopenia can occur, necessitating ongoing evaluation and treatment adjustments.

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Given the variability in presentation and response to treatment, as well as the risks associated with both disease and therapy, evidence-based clinical protocols can assist healthcare providers in balancing the benefits and risks of intervention, reducing morbidity, and improving quality of life for pregnant women with ITP. This article aims to review the current understanding of the pathophysiology, diagnosis, and treatment options for immune thrombocytopenia in pregnancy and to propose a practical clinical protocol for its management.

Methods

This study was conducted as a prospective observational analysis combined with a protocol development phase at the Department of Obstetrics and Hematology in a tertiary care hospital specializing in maternal-fetal medicine. The study period spanned two years, from January 2022 to December 2023. The aim was to develop and validate a clinical protocol for the diagnosis and management of immune thrombocytopenia (ITP) in pregnant women.

Pregnant women diagnosed with thrombocytopenia (platelet count < 100 × 10^9/L) who were referred to the hematology and obstetrics departments were enrolled consecutively. Inclusion criteria were: confirmed pregnancy at any gestational age, platelet count below 100 × 10^9/L on at least two separate tests spaced one week apart, and no other known causes of thrombocytopenia at presentation. Exclusion criteria included: patients with pre-existing hematologic malignancies, systemic lupus erythematosus (SLE) or other autoimmune diseases, preeclampsia, HELLP syndrome, or other medical conditions known to affect platelet counts.

All participants underwent a comprehensive diagnostic evaluation to differentiate ITP from other causes of thrombocytopenia during pregnancy. Initial laboratory investigations included complete blood count with peripheral smear, reticulocyte count, liver and renal function tests, coagulation profile, and tests for viral infections such as HIV, hepatitis B and C. Antinuclear antibody (ANA) testing and direct antiglobulin test (Coombs test) were performed to exclude autoimmune hemolytic anemia or systemic autoimmune diseases.

Bone marrow aspiration was reserved for cases with atypical features, such as abnormal peripheral smear morphology, leukopenia or anemia, or lack of response to standard therapy. Gestational age was confirmed by ultrasonography, and fetal well-being was monitored throughout pregnancy.

Patients were assessed clinically for bleeding manifestations, including petechiae, ecchymosis, mucosal bleeding, and any major hemorrhagic events. Bleeding severity was graded using a standardized bleeding score system. Platelet counts and clinical status were monitored every 1-2 weeks, with more frequent assessments for patients with platelet counts below 30 × 10^9/L or active bleeding.

The clinical protocol was developed based on existing international guidelines (American Society of Hematology, British Society for Haematology), available literature, and expert consensus. Treatment initiation criteria were platelet counts below 30 × 10^9/L or presence of bleeding symptoms irrespective of platelet count. First-line therapy included corticosteroids (prednisone 0.5–1 mg/kg/day) with dose adjustments based on response and side effects.

For patients with inadequate response or corticosteroid contraindications, intravenous immunoglobulin (IVIG) at 1 g/kg daily for two consecutive days was administered. In refractory cases, second-line therapies including rituximab or thrombopoietin receptor agonists were considered, with multidisciplinary team approval.

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Delivery planning involved coordinated efforts between hematologists and obstetricians to maintain platelet counts above 50 × 10^9/L for vaginal delivery and 80 × 10^9/L for cesarean section. Neonates were monitored for thrombocytopenia post-delivery.

Data on demographics, clinical presentation, laboratory values, treatment regimens, and outcomes were systematically recorded in a secured database. Treatment response was defined as an increase in platelet count above 50 × 10^9/L and absence of bleeding. Safety was assessed by monitoring maternal side effects and fetal complications.

Statistical analysis was performed using SPSS version 25.0 (IBM Corp., Armonk, NY). Descriptive statistics summarized patient characteristics and outcomes. Comparisons between treatment groups were made using chi-square tests for categorical variables and t-tests or Mann-Whitney U tests for continuous variables. A p-value of <0.05 was considered statistically significant.

Results

During the study period, 75 pregnant women with thrombocytopenia were initially screened, and after applying exclusion criteria, 62 patients met the inclusion criteria and were enrolled. The mean age of participants was 29.4 ± 5.8 years, with a gestational age at diagnosis averaging 16.2 ± 6.3 weeks. Baseline platelet counts ranged from 8 × 10^9/L to 95 × 10^9/L, with a median of 38 × 10^9/L. All patients underwent thorough diagnostic evaluation to exclude other causes of thrombocytopenia. Peripheral blood smear analysis showed isolated thrombocytopenia without abnormal platelet morphology in 58 patients. Four patients with atypical features underwent bone marrow aspiration, which ruled out malignancies and other hematologic disorders. Viral serologies were negative, and autoimmune markers were positive in six patients without fulfilling systemic lupus erythematosus criteria. Gestational thrombocytopenia was excluded based on platelet counts and clinical findings, confirming immune thrombocytopenia diagnosis in all participants.

Clinically, 64.5% (40 patients) presented with bleeding symptoms at diagnosis, mostly mild mucocutaneous bleeding such as petechiae and ecchymoses, with five patients experiencing moderate mucosal bleeding including epistaxis and gingival bleeding. No major hemorrhagic events were observed at baseline. All patients received treatment according to the developed clinical protocol. Corticosteroids were administered as first-line therapy in 48 patients (77.4%), while 14 patients (22.6%) received intravenous immunoglobulin (IVIG) due to corticosteroid contraindications or resistance. In the corticosteroid group, 79.2% achieved complete response, defined as platelet counts above 50 × 10^9/L within four weeks, with a median response time of 18 days. Eight patients showed partial response, and two were non-responders. Among patients receiving IVIG, 85.7% achieved complete response with a faster median response time of seven days. Two patients required second-line therapies.

Refractory cases totaled six, with four patients treated successfully with rituximab, achieving platelet stabilization above 50 × 10^9/L within six weeks, while two patients responded to thrombopoietin receptor agonists. Maternal bleeding complications during pregnancy and delivery were minimal, with platelet counts maintained above the threshold levels necessary for safe vaginal delivery (50 × 10^9/L) and cesarean section (80 × 10^9/L). Neonatal outcomes were favorable, with no cases of severe thrombocytopenia or intracranial hemorrhage reported. Mild transient neonatal thrombocytopenia was noted in five newborns, resolving spontaneously within two weeks postpartum.

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Regarding safety, corticosteroid therapy was associated with gestational diabetes in five patients and hypertension in three, while IVIG was generally well tolerated with only mild infusion reactions in three cases. No serious adverse events occurred. Overall, the clinical protocol proved feasible and safe in clinical practice, yielding high treatment response rates and low rates of complications, confirming its applicability for managing immune thrombocytopenia during pregnancy.

Discussion

Immune thrombocytopenia (ITP) during pregnancy remains a complex condition requiring careful diagnostic evaluation and individualized treatment approaches to minimize risks to both the mother and fetus. The results of this study demonstrate that a structured clinical protocol incorporating established diagnostic criteria and a stepwise treatment algorithm can effectively guide clinicians in managing ITP in pregnant patients, ensuring favorable outcomes and minimizing complications.

The diagnostic process outlined in the protocol successfully distinguished ITP from other causes of thrombocytopenia, such as gestational thrombocytopenia and secondary autoimmune or hematologic conditions. This differentiation is critical, as the management and prognosis vary significantly between these conditions. In particular, the use of thorough clinical assessment combined with targeted laboratory testing, including peripheral smear, autoimmune markers, and selective bone marrow examination, allowed for accurate diagnosis in the majority of cases. This approach aligns with recommendations from international hematology societies, emphasizing the need for exclusion of secondary causes before confirming ITP.

Our findings corroborate previous reports indicating that corticosteroids remain the cornerstone of first-line therapy in pregnant women with ITP. The high response rate observed with corticosteroids in this study (79.2%) supports their efficacy in increasing platelet counts while providing a relatively safe profile when used judiciously during pregnancy. However, the associated maternal side effects, including gestational diabetes and hypertension, underscore the importance of careful monitoring and dose adjustment to mitigate these risks. The protocol's inclusion of IVIG as an alternative or adjunctive therapy provided an effective option for patients who were steroid-resistant or had contraindications, with a faster median time to platelet recovery noted in the IVIG group. This finding is consistent with the literature that supports IVIG's role in rapid platelet count elevation, especially in cases where urgent intervention is required.

Refractory cases posed a significant clinical challenge, and the protocol's recommendation to consider second-line agents such as rituximab and thrombopoietin receptor agonists proved beneficial. Although data on the safety of these agents in pregnancy remain limited, their use in selected cases under multidisciplinary supervision facilitated platelet stabilization and reduced bleeding risk. These findings highlight the need for ongoing research into novel therapeutic options and their safety profiles in pregnant patients with refractory ITP.

The favorable maternal and neonatal outcomes observed in this study are particularly noteworthy. Maintaining platelet counts above critical thresholds during delivery is essential

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to minimize hemorrhagic complications. The protocol's coordinated care approach between hematologists and obstetricians ensured appropriate timing and preparation for delivery, with no major maternal bleeding events reported. Neonatal monitoring identified a small proportion of infants with transient thrombocytopenia, which resolved without intervention, reflecting the known risk of passive antibody transfer. This emphasizes the importance of neonatal platelet surveillance and readiness to manage potential complications.

The safety profile of the treatments used within the protocol supports their continued use in pregnancy, albeit with vigilance for adverse effects. The balance between treatment benefits and potential risks requires individualized decision-making, taking into account disease severity, gestational age, and patient preferences. Furthermore, the protocol facilitates patient counseling and education, empowering women to participate actively in their care, which can improve adherence and outcomes.

Conclusion

In conclusion, the clinical protocol developed and validated through this study offers a practical and evidence-based framework for diagnosing and managing immune thrombocytopenia in pregnancy. It enables effective treatment initiation, appropriate monitoring, and timely escalation of therapy while minimizing risks to both mother and child. Future multicenter studies with larger cohorts are needed to refine these recommendations further and explore long-term maternal and neonatal outcomes. Continued collaboration among hematologists, obstetricians, and pediatricians will remain essential to optimize care for this vulnerable population.

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