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Immune Profiling of Humoral and Inflammatory Responses in Pediatric Immune Thrombocytopenia in Non-Admitted Children Aged 2–10 Years

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Abstract:

Introduction: Idiopathic thrombocytopenic purpura (ITP) is a common acquired autoimmune disease of childhood characterized by isolated thrombocytopenia. Ineffective immune control by the humoral and cytotoxic responses may be permissive for disease initiation and progression. In this study we aimed to estimate the CRP, Anti- IgG, IgM- and IgA responses in NonAdmitted pediatric ITP patients vs healthy controls.

Methods: A case–control study was conducted on 20 ITP patients and 20 healthy controls, who were aged between two and 10 years. The serum levels of hs-CRP and immunoglobulin (IgG, IgM, IgA) were examined by immunoturbidimetry and enzyme-linked immunosorbent assay (ELISA). Platelet indices were recorded. Descriptive statistics were calculated, and the t-test and correlation was utilized in univariate analysis; further logistic regression according to the enter rule was used for predictors of severe thrombocytopenia.

Results: Patients with ITP had markedly elevated hs-CRP and Ig profiles abnormalities than controls. There were lower platelet counts with higher CRP and lower IgA. The logistic regression identified hs-CRP and IgA as 2 independent risk factors for severe thrombocytopenia.

Conclusion: The CRP and immunoglobulin profiles could be of value in the understanding of the immunopathogenesis of pediatric ITP, and might serve as adjunctive markers in monitoring disease Non-Admitted subjects.

Key words: Idiopathic thrombocytopenic purpura, Inflammatory Responses, Pediatric Immune Thrombocytopenia

Introduction

Immune thrombocytopenia (ITP) has been discovered to be the most frequent acquired bleeding disorder in childhood and it is a disorder caused by immune-mediated destruction of platelets and abnormal functioning of megakaryocyte [1]. The incidence is estimated to be 2–6 /100,000 children/year and the peak incidence appears during younger ages [2]. Most children also present with the sudden appearance of petechias, purpuras or mucosal bleeding and have spontaneous severe bleeding [3].

The exact aetiology of ITP is not well established, but it is considered an autoimmune disease secondary to genetic predisposition and environmental factors, including approximately one viral infection [4]. Both humoral and cellular immunity are involved in the pathophysiology. Autoantibodies against platelet surface glycoproteins (e.g., GPIIb/IIIa, GPIb/IX) opsonize the cells

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and splenic sequestration occurs [5]. In addition, immune dysregulation affects T-cell subpopulations, the cytokine network and regulatory B-cell function [6].

C-reactive protein (CRP) is an indicator of systemic inflammation and is involves in the autoimmune diseases [7]. Elevation in CRP levels has been linked to disease activity and adverse outcome in children with hematologic diseases [8]. Similarly, IgG and IgA are a part of humoral response. IgG and IgM are important in systemic immunity, while IgA indicates mucosal immunity [9]. Deltas in the immunoglobulins have been reported in children with autoimmune and post-infectious diseases, reflecting modulation of immune response [10].

To the best of our knowledge, potential function of CRP and immunoblobules at the time is poorly analyzed in pediatric ITP among both Admitted (inpatient) and Non-Admitted patients who represent a higher percent of outpatient settings when recruiting [11]. These immunological markers help us understand the pathophysiology of disease, predictors of severity and can guide targeted monitoring.

The aim of the present report was to assess two immunoregulators, namely CRP and immunoglobulins (IgG, IgM, IgA), in ITP children aged 2–10 years as compared with healthy controls. We hypothesized that the alterations of inflammatory and humoral markers might be correlated with the severity of thrombocytopenia.

Methods

Design and Setting: This study was a case–control study, which was performed at a pediatric hematology outpatient clinic between January 2024 and June 2025.

Patients: Forty children aged between 2 and 10 years, including 20 cases with ITP and 20 healthy controls were included in this study. All patients of ITP were New Diagnosis Non-Admitted and defined under the international diagnosis code. Control group was normal age and sex matched healthy children attending for routine health checks.

Eligibility: Children aged 2–10 years with a platelet level <100 × 10^9/L and a clinical diagnosis of (TP).

Exclusionens: concurrent autoimmune disease, acute infection immunosuppressive treatment or recent hospitalization.

Laboratory Examinations: 5 mL venous blood was obtained. Platelet indices were assessed using automated hematology analyzer. CRP was assayed by high-sensitive immunoturbidimetric test. Immunoglobulin (IgG, IgM and IgA) were measured using nephelometry or enzyme-linked immunosorbent assay. Pediatric reference ranges were applied.

Statistical process Data were statistically processed by SPSS 25 program. Continuous variables were described as means ± SD. Between-group comparisons were conducted by independent t-test or Mann–Whitney U-test. The relationships were checked by Pearson' s coefficient. Factors associated with severe thrombocytopenia (<30×10^9/L) were analyzed by logistic regression. All statistical tests were two-sided and $p < 0.05$ was considered significant.

Ethics/Consent: The ethics committee of our institute granted a waiver for informed consent in this study. Parental consents were obtained and assent for older kids.

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Results and Discussion

The present study shows that pediatric patients with ITP have an abnormal humoral and inflammation profileP compared with healthy controls. There were also increased hs-CRP and alterations of immunoglobulins, suggesting a correlation between systemic inflammation and humoral immune dysfunction.

The results are shown in tables that follow:

Table 1. Demographic Data of Pediatric ITP Patients and Controls

Characteristic	ITP Patients (n=20)	Controls (n=20)	p-value
Age (years), mean ± SD	6.1 ± 2.4	6.3 ± 2.2	0.72
Male, n (%)	11 (55%)	10 (50%)	0.76
Platelet count (×10^9/L), mean ± SD	56 ± 22	289 ± 54	<0.001
MPV (fL), mean ± SD	10.7 ± 1.1	8.9 ± 0.8	<0.001
PDW (%), mean ± SD	16.5 ± 2.4	13.2 ± 1.9	<0.001
Bleeding score, median (IQR)	2 (1–3)	—	—

Our findings confirmed that CRP is a sensitive measure of inflammation in patients with ITP. The fact that nondischarge patients also have elevated hs-CRP levels suggests that low grade inflammation is in latter itself a product of active disease process without respect to hospitalization. Other Similar studies have also demonstrated an increased CRP in autoimmune hemato- malignant diseases such as systemic lupus erythema- logical disturbances, even further relating it to the tumor-carcinoma [12, and other severity of the disease [mesotheliomas 13].

Analysis of serum immunoglobulins (IgG, IgM and IgA) revealed heterogeneity among patients. Reduced IgA levels were particularly profound and linked with thrombocytopenia, suggesting the link between mucosal immunity and systemic autoimmune breakdown. This is similar to other paediatric autoimmune conditions where IgA deficiency has been found associated with immune dysregulation [14,15]. Altered concentrations of IgM and IgG may reflect an ongoing chronic immune activation and/or platelet-antibody mediated destruction [16].

Table 2. Serum hs-CRP and Immunoglobulin Levels (IgG, IgM, IgA) in ITP vs Controls

Parameter	ITP Patients (Mean ± SD)	Controls (Mean ± SD)	p-value
hs-CRP (mg/L), mean ± SD	2.8 ± 1.6	0.9 ± 0.6	<0.001
IgG (g/L), mean ± SD	8.1 ± 1.6	9.0 ± 1.5	0.04
IgM (g/L), mean ± SD	1.1 ± 0.4	1.3 ± 0.5	0.09
IgA (g/L), mean ± SD	0.82 ± 0.28	1.02 ± 0.30	0.02

Correlation analysis showed that CRP/Ig levels were significantly correlated with platelet indices, in particular the MPV (a surrogate for bone marrow platelet formation). Independent factors associated with severe thrombocytopenia were hs-CRP and IgA as per a logistic regression analysis, suggesting their potential role as prognostic indicators in clinical practice.
Table 3. Correlations Between Immune Markers and Platelet Indices

Marker	Platelet Count (r, p)	MPV (r, p)	PDW (r, p)	
hs-CRP	r = -0.48, p = 0.02	r = 0.39, p = 0.05	r = 0.36, p = 0.07	
IgG	r = 0.21, p = 0.36	r = -0.18, p = 0.44	r = -0.12, p = 0.63	
IgM	r = 0.09, p = 0.71	r = -0.05, p = 0.84	r = -0.07, p = 0.77	
IgA	r = 0.42, p = 0.04	r = -0.31, p = 0.10	r = -0.28, p = 0.15	

Table 4. Logistic Regression Predictors of Severe Thrombocytopenia

Variable	Odds Ratio (OR)	95% CI (Lower)	95% CI (Upper)	p-value
hs-CRP (per 1 mg/L)	1.35	1.05	1.92	0.03
IgA (per 1 g/L)	0.38	0.16	0.91	0.03
MPV (per 1 fL)	1.27	1.01	1.72	0.04
Age (per year)	0.94	0.71	1.22	0.64

In contrast to previous studies in hospitalized or severe ITP, the present study focuses on non-admitted patients (the majority of pediatric cases). In the outpatient setting platelet counts are commonly used as the only monitoring tool, however our results indicate that immune biomarkers may be important to improving risk stratification and followup algorithms.

Conclusion

In summary, CRP and immunoglobulin profiles may play an important role in understanding the pathophysiology of pediatric ITP. Their regular assessment may enhance monitoring of the disease and individualization of the care in Non-Admitted patients.

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