



The Role of Serum Interleukins and PTPN22 in the Pathogenesis and Progression of Immune Thrombocytopenia

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10.18805/ajdfr.DRF-574

ABSTRACT

Background: Immune thrombocytopenia (ITP) is a common acquired hematologic autoimmune illness. Objectives: this work goals to examine the role of interleukins (ILs) and polymorphisms of PTPN22 gene in the progression and pathogenesis of ITP.

Methods: 50 ITP patients were included. Human serum levels of antinuclear antibodies (ANA), anti-platelet antibody (PA-Ab) and IL-40 were measured using enzyme linked immunosorbent assay (ELISA). Gene expression of Protein tyrosine phosphatase non-receptor type 22 (PTPN22) were determined using Real-time polymerase chain reaction (RT-PCR), while the sequencing of this gene was determined using Sanger method and genotyping was detected using conventional PCR.

Result: No significant variations were observed in serum level of ANA, PA-Ab and IL-40, PTPN22 gene expression and its single nucleotide polymorphism (rs2488457) in acute and chronic cases of ITP.

Key words: ANA, ELISA, Gene expression, IL-40, ITP, RT-PCR.

INTRODUCTION

Immune thrombocytopenia (ITP) is an illness of raised peripheral platelets' damage or/and declined or insufficient production of platelets. This illness is a rare autoimmune illness with an occurrence approximately 3/100,000 individual-years, with a peak among males older than seventy-five years (9/100,000 individual-years). Factors originating ITP are unidentified; however, seasonal variations have been indicated with a raised occurrence throughout winter, supposing a role for viral infectious illnesses. Nevertheless, both chronic (>12 months after diagnosis) and persistent ITP (>3 months after diagnosis) affect 70% of adult individuals and are less susceptible to such variations, supposing the involvement of other parameters (Audia *et al.*, 2021; Abbas *et al.*, 2024; Al-Naddawi *et al.*, 2014; Al-Aqabi and Alwan, 2010).

The ITP is an illness that may be chronic or transient and it is categorized by The International Working Group in ITP as primary or secondary according to the presence of a predisposing condition or an apparent precipitating parameter. In adults, 80% of newly detected individuals have primary ITP, which is marked by isolated thrombocytopenia. Secondary ITP is activated or linked with a hematological condition (autoimmune lymphoproliferative syndrome, lymphoma, or chronic lymphocytic leukemia), an autoimmune illness (rheumatoid arthritis, or lupus erythematosus), a chronic infectious illness (hepatitis C virus-HCV, or *Helicobacter pylori*), or subsequent therapy with drugs like quinidine and heparin (Mititelu *et al.*, 2024; Ahmed *et al.*, 2024).

Main factors responsible for abnormalities of ITP are platelet-specific glycoproteins and autoantibodies targeting megakaryocytes as well as cytotoxic T cells directly acting on platelets. Despite the fact that antibodies to specific glycoproteins of platelet membranes are exist in the

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How to cite this article: Lamam, S.N. and Ibraheem, S.R. (2025). The Role of Serum Interleukins and PTPN22 in the Pathogenesis and Progression of Immune Thrombocytopenia. *Asian Journal of Dairy and Food Research*. 1-9. doi: 10.18805/ajdfr.DRF-574.

Submitted: 15-07-2025 **Accepted:** 30-09-2025 **Online:** 13-10-2025

majority of patients, the specific mechanism by which autoantibodies toward platelets are formed remains an unknown. Besides, the precursor of platelet in the bone marrows, megakaryocytes, may suffer distribution by autoantibodies of platelet which limits their synthesis of platelet. (Bussel *et al.*, 2021; Zakaria *et al.*, 2023). Immunologically, T cells' dysfunction in individuals with ITP may result in tolerance loss, which have a vital function in the pathogenesis of this disease. Besides, T lymphocytes polarize into response of helper T-1 marked principally via the presence of tumour necrosis factor (TNF)- α and interferon- γ as well as response of helper T-2 forms IL-10, IL-4 and IL-13. Several serum interleukins, IL-11 and IL-1 β , could be vital biomarkers in the ITP diagnosis. (Zhan *et al.*, 2021; Elsaid *et al.*, 2022; Al Shami *et al.*, 2024; Lubis *et al.*, 2024).

In this context, this work goals to examine the role of interleukins (ILs), including IL-40, in addition to polymorphisms of PTPN22 gene in the progression and pathogenesis of ITP.

MATERIALS AND METHODS

Subjects

A total of 50 ITP patients (27 acute cases and 23 chronic cases) were included. The blood sample collected from Central Teaching Hospital pediatric (Baghdad/ Iraq) from February to August 2024. The physician was diagnosed the patients with ITP using complete blood count (CBC) and blood film.

Included criteria

These cases comprised of 22 females and 28 males with ages ranging from 1 to 15 years.

Excluded criteria

Each individual with age out of 1 and 15 years, not have ITP, having disease rather than ITP.

Collection of blood samples

From each ITP patient, a 5ml of samples of blood were obtained and separated into 3 parts: 2 ml of blood samples were kept in EDTA at -20°C till usage for genotyping. A 2.5 ml of blood was obtained in a gel plane tube and serum separated directly via centrifugation and transported into another plane tube and kept at -20°C for immunologic tests. A 0.5 ml blood was added to the Eppendorf tube containing 0.5 ml of TRIzol™ Reagent and kept at -20°C for molecular analysis.

Immunological assay

Serum levels of ANA and IL-40 were measured using ELISA kit (Sunlong/ China), while serum level of PA-Ab was measured using ELISA kit (Shanghai YL Biont/China).

Molecular study

Gene expression determination

RNA extraction

The TRIzol™ Reagent technique was utilised to isolate RNA. The concentration of extracted RNA was measured using a Quantus Fluorometer to assess the quality of samples for future usage. The findings showed that the RNA concentrations varied from 6 to 651 ng/L.

Primer design and preparation

The β -Globin gene was obtained from the National Center for Biotechnology Information Gene Bank (NCBI). The Premier 3 software was utilized to design *PTPN22* gene primers (Macrogen Company, Korea), as follows: β -Globin-reverse (5'-CAACTTCATCCACGTTTACC-3') and β -Globin-forward (5'-ACACAACTGTGTTCACTAG C-3'), with lengths of 20 bp and annealing temperature of 65°C while *PTPN22*-reverse (5'-GTAGCTGGAATCCTCATCAGAGG-3') and *PTPN22*-forward (5'-ACAACTGT GGCTGAGAAGCC CA-3') with length of 22 and 23 bp, respectively and annealing temperature of 60°C.

RT-qPCR

GoTaq® qPCR Master Mix Real time (Promega/USA) was utilized to accomplish the whole reaction, from synthesis

of cDNA to amplification of PCR. A total volume of 1 μ l of RNA had to be reverse-transcribed and the reaction volume was 10 μ l. The reaction mixture was modified to a total volume of 10 μ l, following the manufacturer's recommendation. It consisted of 5 μ l qPCR Master Mix (1X), 0.3 μ l of each primer (10 μ M), 3.4 μ l nuclease-free water and 1 μ l cDNA (5-15 ng/ μ l). The mix was transferred to an RT-qPCR program (BioMolecular System, Australia) that was programmed for each step (temperature; time m:s; cycle), as follows: RT-Enzyme Activation step (37; 15:00; 1), Initial Denaturation step (95; 05:00; 1), Denaturation step (95; 00:20; 40), Annealing step (60 or 65; 00:20; 40), Extension step (72; 00:20; 40).

Gene expression

The $\Delta\Delta C_t$ method (Livak *et al.*, 2001). was utilized to normalize the expression data for *PTPN22* versus β -Globin and the results were presented as changes of folding ($2^{-\Delta\Delta C_t}$) in expression of genes.

Genotyping determination

DNA extraction

Genomic DNA was isolated from blood sample according to the protocol ReliaPrep™ Blood gDNA Miniprep System as manufacturer's recommendations (Promega/USA). As a means of gauging the sample's quality for further uses, the Quantus Fluorometer measured the concentration of extracted DNA. gDNA concentrations were ranged between 10-22 ng/ μ l.

SNP genotyping

To amplify the (782 bp) region of *PTPN22* gene SNPs (rs2488457), conventional PCR was utilized. Reverse primer (5' - CAGGAAACAGCTATGACGACCAGACAGTT AGCTCAATAC -3') and forward primer (5' - TGTA AAAA CGAC GGCCAGTCGTTACTTAGA GCAGCAAGAA - 3') of *PTPN22* gene SNP (rs2488457) with length of 39 bp and annealing temperature of 50°C. The whole volume for the PCR reaction was 25 μ l, including 12.5 μ l of GoTaq green Master mix, 7.5 μ l of nuclease-free distilled water, 1 μ l of each primer, Forward and Reverse (10 μ M) and 3 μ l of DNA sample (20-29 ng). To confirm the presence of amplification after amplification of PCR, gel electrophoresis of agarose (1.5%) was utilized. The mix was transferred to a conventional PCR program (BioMolecular System, Australia) that was programmed for each step (temperature; time m:s; cycle), as follows: initial denaturation step (95; 05:00; 1), denaturation step (95; 00:30; 30), annealing step (55; 00:30; 30), extension step (72; 00:45; 30), final extension step (72; 07:00; 1), hold step (10; 10:00, 1).

Standard sequencing

The PCR products were delivered to Macrogen Corporation - Korea for Sanger sequencing utilising an automated DNA sequencer called an ABI3730XL. Geneious software was utilized to analyse the findings after receiving them over email.

Statistical analysis

Data analysis was carried out with the help of GraphPad Prism 7.0. For parametric data, an unpaired t-test was used; for non-parametric data, a Mann-Whitney U test was used to determine the likelihood. To determine the likelihood of categorical data, either the chi-square or Fisher exact tests were utilized. The spearman correlation test was used to determine the level of correlation between the values. In order to do ROC analysis, the SPSS statistical tool was used. A statistically significant difference was defined as a P value lower than 0.05.

RESULTS AND DISCUSSION

General characteristics

The comparison among acute and chronic individuals with ITP yielded the following results: Age was not significantly different among acute and chronic individuals with ITP (5.6 ± 3.81 vs. 7.54 ± 3.55 years, $p=0.0749$). Sex distribution was also comparable among the two groups (62.96% male in acute vs. 47.83% in chronic, $p=0.3926$). BMI was similar among acute and chronic individuals with ITP (32 vs. 32.7, $p=0.6261$). As expected, the period of illness differed, with 33.34% of acute individuals with ITP having symptoms for <1 month and 78.26% of chronic individuals with ITP having symptoms for <1 year. Treatment status differed, with all chronic individuals with ITP receiving treatment and 25.93% of acute individuals with ITP not receiving treatment, as represented in Table 1.

Hematological study

Hematological parameters, including mean $\pm$ SD of RBC (4.78 ± 0.483 vs. $4.64 \pm 0.41 \times 10^6/\mu\text{L}$, $p=0.2685$) and Hb (12.56 ± 1.43 vs. 12.34 ± 1.68 g/dl, $p=0.631$) as well as median of WBC (9.9 vs. $8.9 \times 10^3/\mu\text{L}$, $p=0.674$) and PLT (186 vs. $72 \times 10^3/\mu\text{L}$, $p=0.2893$) detected no significant variations among acute and chronic individuals with ITP, respectively, as represented in Fig 1.

Serological study

The comparison among acute and chronic individuals with ITP revealed the following results: ANA levels were not

significantly different among acute and chronic individuals with ITP (8.2 vs. 4.7, $p=0.3225$). IL-40 levels detected a trend towards being greater in acute individuals with ITP, but the variation did not reach statistical significance (10.5 vs. 9.04, $p=0.0676$). PA-Ab levels were significantly greater in acute individuals with ITP compared to chronic individuals with ITP (16.6 vs. 9.5, $p=0.0233$), as represented in Fig 2.

Analyses evaluating the relative strengths of ANA, PA-Ab and IL-40 as diagnostic tools for differentiating between acute and chronic ITP showed mixed results. There was no statistically significant difference between ANA and chance, but the AUC of 0.603 was good and the sensitivity was high at 84.62% with a poor specificity of 50%. There is modest diagnostic potential for IL-40, as it produced a respectable AUC of 0.651, reasonable sensitivity (60.87%) and specificity (66.67%) and a p -value (0.0674) that is approaching towards significance. PA-Ab shown promising biomarker potential with an AUC of 0.689, which was statistically significant ($p = 0.0239$) and had a well-balanced sensitivity (69.57%) and specificity (66.67%), as represented in Fig 3.

Molecular study

Gene expression

The comparison among acute and chronic individuals with ITP detected that *PTPN22* expression levels were not significantly different among the two groups (0.34 vs. 0.225, $p=0.7799$). The wide range of expression levels in both groups (0.01-2.84 in acute and 0.01-3.41 in chronic) suggests variability in *PTPN22* expression among individuals, but overall, the median expression levels were comparable among acute and chronic individuals with ITP, as represented in Table 2.

The study found that *PTPN22* expression fold is not a reliable biomarker for distinguishing between acute and chronic individuals with ITP. The area under the curve (AUC) was 0.527, which is considered "unsatisfactory" and not significantly different from random chance (p -value 0.7726). The optimal cut-off value had a sensitivity of 66.67% and specificity of 52.17%, which is not sufficient for a reliable diagnostic test, as represented in Fig 4.

Table 1: Demographic parameters and medical history of acute and chronic cases with ITP.

Characteristics		Individuals with ITP		p-value
		Acute (n=27)	Chronic (n=23)	
Age (years), mean $\pm$ SD		5.6 ± 3.81	7.54 ± 3.55	0.0749 NS
Sex, n (%)	Male	17 (62.96)	11 (47.83)	0.3926 NS
	Female	10 (37.04)	12 (52.17)	
BMI, median (range)		32 (13.9-72.8)	32.7 (17-62.4)	0.6261 NS
Period of illness, n (%)	< 1 Month	9 (33.34)	0 (0)	-
	< 1 Year	17 (62.96)	5 (21.74)	
	≥ 1 Year	1 (3.7)	18 (78.26)	
Treatment, n (%)	Yes	20 (74.07)	23 (100)	-
	No	7 (25.93)	0 (0)	

*BMI: Body mass index; ITP: Immune thrombocytopenia; p: Probability; NS: Non-significant.

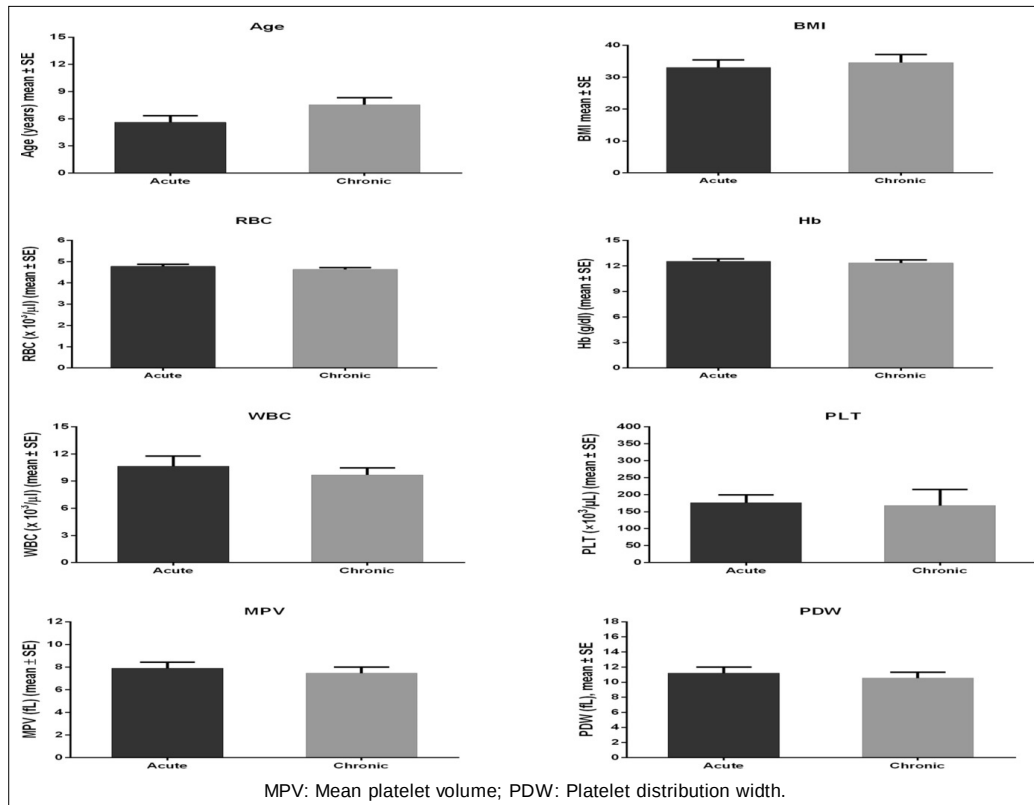


Fig 1: Hematological parameters among acute and chronic cases of ITP.

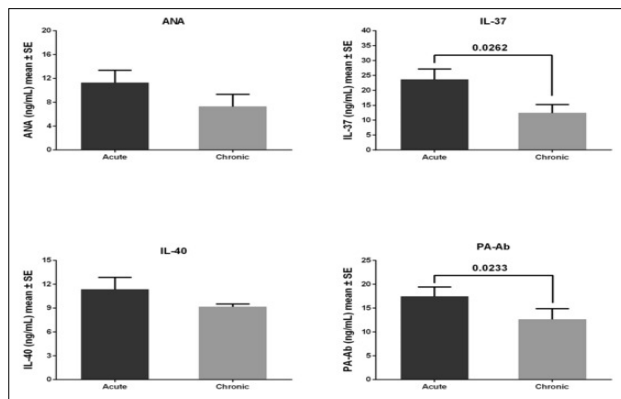


Fig 2: Serological parameters of acute and chronic cases with ITP.

Genotyping

The PCR amplification of rs2488457 specific region were performed and the results, as represented in Fig 5, indicated single band of 782 bp of rs2488457 for patients with ITP.

Sanger sequencing method were utilized in order to estimate the sequence of each SNP (rs2488457) in *PTPN22* gene, as represented in Fig 6.

The comparison of rs2488457 genotype frequencies among acute and chronic individuals with ITP detected no significant variation ($p=0.4996$). The distribution of genotypes was similar among the two groups, with homozygous wild-type being the most common genotype

in both acute (55.6%) and chronic (69.6%) individuals with ITP, followed by heterozygous genotypes (37% in acute and 21.7% in chronic), as represented in Table 3.

Correlation study

The analysis of *PTPN22* expression based on rs2488457 genotype detected no significant variations in both acute and chronic individuals with ITP. In acute individuals with ITP, the median *PTPN22* expression levels were 2.84 for the wild-type genotype (limited to one value), 0.34 for the homozygous genotype and 0.19 for the heterozygous genotype ($p=0.7965$). In chronic individuals with ITP, the median *PTPN22* expression levels were 0.495 for the wild-type genotype, 0.165 for the homozygous genotype and 0.295 for the heterozygous genotype ($p=0.4313$), as represented in Table 4.

The correlation analysis in chronic individuals with ITP revealed several significant relationships. Age detected a high negative correlation with BMI ($r = -0.72$, $p<0.0001$). ANA levels detected significant high positive correlations with IL-40 ($r = 0.63$, $p<0.05$), as represented in Table 5.

This study focuses on the role of immunological biomarkers (IL-40) and genetic marker (*PTPN22* gene) in incidence of acute and chronic ITP cases.

Depending these outcomes, the difference in *PTPN22* expression of acute and chronic cases was not statistically significant. This contrasts with findings in other autoimmune and inflammatory diseases, where *PTPN22* expression

tends to be elevated. For instance, (Ruan *et al.*, 2022). reported an upregulation of *PTPN22* in immune cells within the aortic tissue of patients with abdominal aortic aneurysm (AAA), suggesting a pro-inflammatory role. Similarly, (Hassan *et al.*, 2024). observed significantly increased *PTPN22* expression in individuals with autoimmune inflammatory diseases (AID), further supporting its involvement in heightened immune response. On the other hand, (Moneim *et al.*, 2023) did not observe a significant difference in *PTPN22* mRNA expression between systemic lupus erythematosus (SLE) patients and healthy controls, indicating disease-specific variation in gene regulation. In addition, gene expression of *PTPN22* decreased in patients of SLE in compared to healthy controls (HCs)

(Román-Fernández *et al.*, 2022). Moreover, (Menchaca-Tapia *et al.*, 2023). reported a remarkable 17-fold increase in *PTPN22* expression in patients with primary Sjögren's syndrome (pSS), highlighting a strong association between the gene and glandular autoimmunity. Similarly, (Ramírez-Pérez *et al.*, 2019). found that *PTPN22* was linked to higher gene expression in rheumatoid arthritis (RA), reinforcing the gene's role in T-cell regulation and autoimmunity. These findings collectively suggest that *PTPN22* may act as a regulatory hub in immune-mediated diseases, with expression levels varying depending on the underlying pathophysiology of each condition. *PTPN22* is expressed in most human leukocyte types, including neutrophils, CD4+ T cells, dendritic cells, macrophages, monocytes,

Table 2: Gene expression of *PTPN22* among acute and chronic cases with ITP.

Characteristics	ITP (n=50)		p-value
	Acute (n=27)	Chronic (n=23)	
<i>PTPN22</i> expression foldmedian (range)	0.34 (0.01-2.84)	0.225 (0.01-3.41)	0.7799 NS

*ITP: Immune thrombocytopenia; p: probability; NS: non-significant; *PTPN22*: Protein tyrosine phosphatase non-receptor type 22.

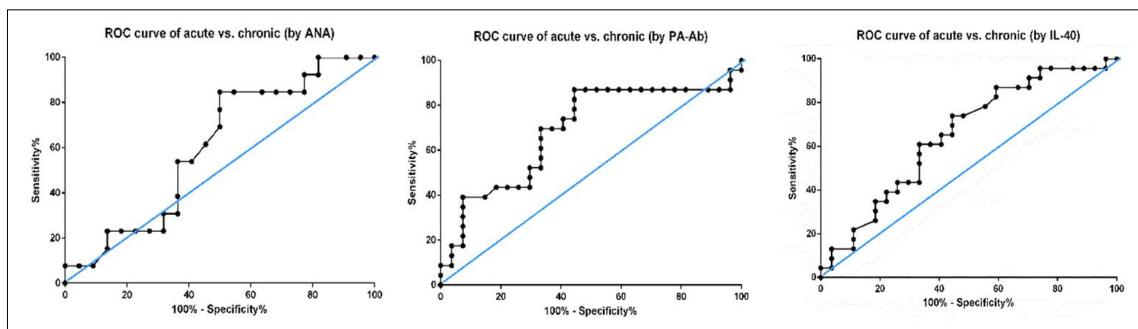


Fig 3: ROC of PA-Ab, ANA and IL-40 among acute and chronic cases with ITP.

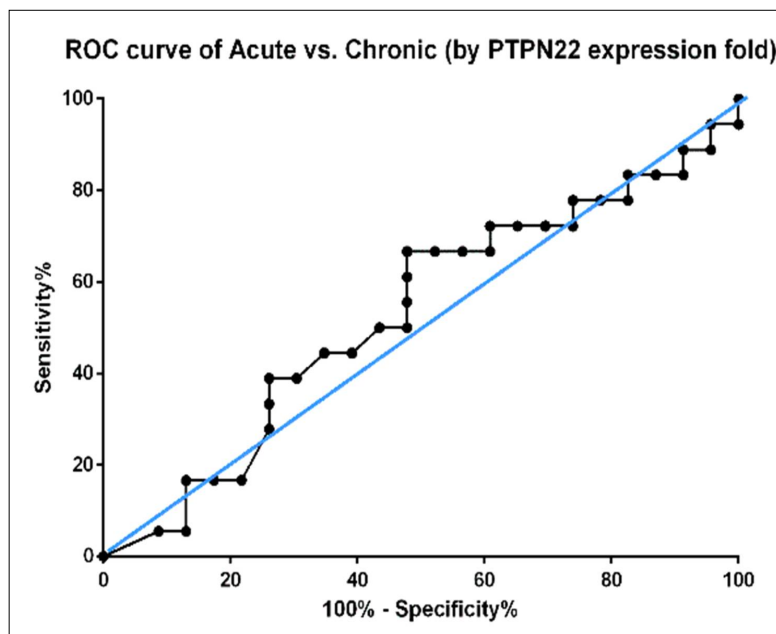


Fig 4: ROC analysis of *PTPN22* gene expression among acute and chronic cases with ITP.

NK cells, B cells and CD8+ T cells. Of these cells, PTPN22 has the highest expressions in activated naïve CD4+ and CD8+ T cells, followed by B cells and NK cells, with lower levels in monocytes (Armitage *et al.*, 2021). The *PTPN22* gene plays a significant role in immune regulation and is

implicated in various diseases, particularly autoimmune disorders. Variants in this gene can lead to altered protein function, which affects T-cell activation and signaling pathways (Brownlie *et al.*, 2024). This dysregulation can increase susceptibility to autoimmune diseases such as

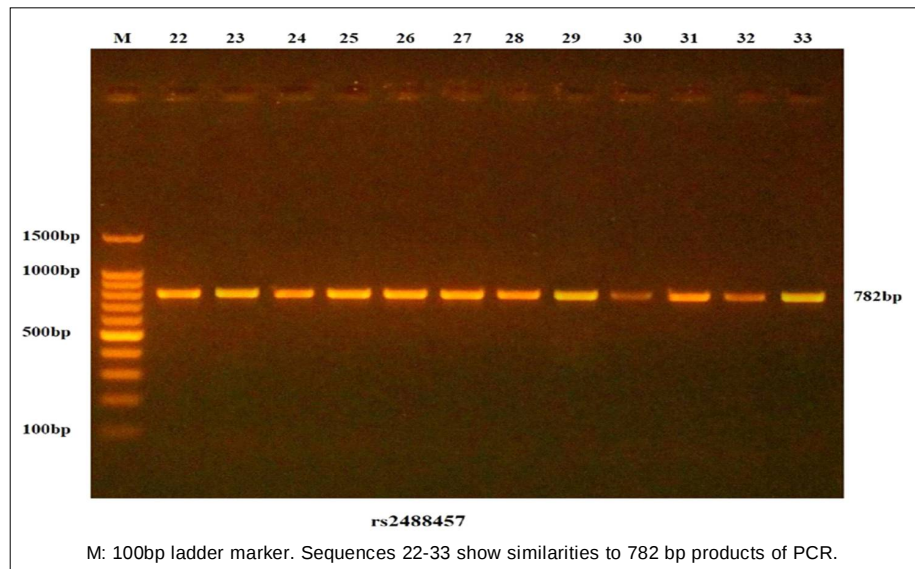


Fig 5: The outcomes of the specific area amplification of rs2488457 were processed utilising gel electrophoresis of 1.5% agarose stained with Eth.Br.

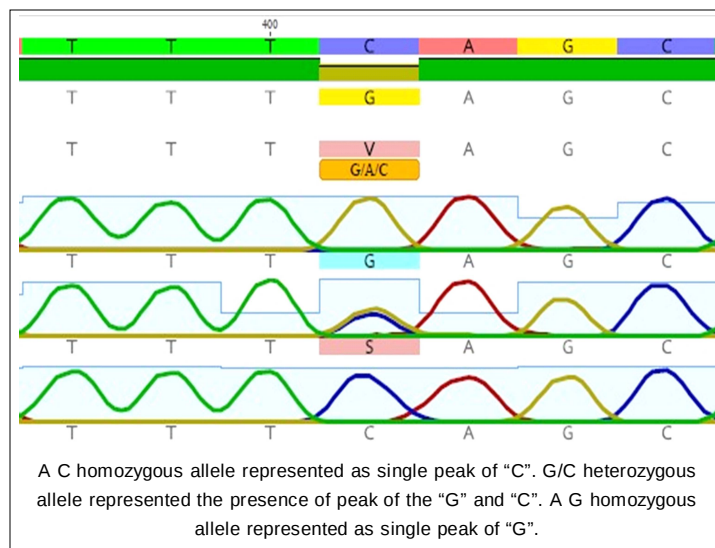


Fig 6: Sanger sequencing analysis of *PTPN22* gene rs2488457 SNP.

Table 3: Frequency of rs2488457 among acute and chronic with ITP.

Characteristics		rs2488457 genotyping, n (%)			p-value
		Wild GG	Homo CC	Hetero GC	
Groups	Acute	2 (7.4)	15 (55.6)	10 (37)	0.4996 NS
	Chronic	2 (8.7)	16 (69.6)	5 (21.7)	

*ITP: Immune thrombocytopenia; p: Probability; NS: Non-significant; Homo: Homozygous genotype; Hetero: Heterozygous genotype.

rheumatoid arthritis (Budlewski *et al.*, 2023) type 1 diabetes (Newman *et al.*, 2023) and SLE (Ates *et al.*, 2025) where the immune system mistakenly attacks the body's own tissues.

This study and (Tian *et al.*, 2022) focus on the association of the *PTPN22* gene SNP (rs2488457) with ITP. Tian *et al.* found that carriers of genotypes of GG were 1.51 times more susceptible to ITP than carriers of CC, with a significant *p*-value of 0.009. This suggests that while this study observed no difference in genotype frequency, Tian *et al.* provided evidence of a meaningful association with susceptibility, highlighting a potential inconsistency in findings (Zhang *et al.*, 2022; Bhat *et al.*, 2024) identified a significant relationship between rs2488457 polymorphisms and uveitis susceptibility, showing that the C allele was associated with increased risk (OR = 1.18, *p* = 0.029). This contrasts with this study, which reported no significant differences in the distribution of genotypes among both cases with ITP. The study by (Menchaca-Tapia *et al.*, 2023). found no significant differences in genotype frequencies for rs2488457 between primary Sjögren's syndrome patients and HCs, aligning with the lack of significant findings in this study regarding ITP. This suggests a possible commonality in that both immune disorders may not exhibit strong associations with this particular SNP, indicating a need for further investigation into genetic risk factors for these conditions.

(Kaymaz *et al.*, 2023) examined the frequency of the G allele in lung sarcoidosis, reporting a G allele frequency of 67%, whereas this study found 8% of ITP patients with the GG genotype. The stark difference in genotype frequencies suggests that the impact of rs2488457 may be disease-specific. This reinforces the notion that genetic susceptibility can vary significantly across different diseases, necessitating a tailored approach to genetic research in immune disorders. (Jiménez-Becerra *et al.*, 2024; Ngurthankhumi *et al.*, 2024) reported a range of 36% to 48% for the risk allele PTPN22 rs2488457G in systemic lupus erythematosus. In contrast, this study reported a lower prevalence of the GG genotype in ITP. The variation in allele distribution highlights the complexity of genetic influences on autoimmunity and suggests that while certain SNPs may be implicated in multiple conditions, their prevalence and impact can differ markedly.

Lu *et al.* (2022) found no contribution of rs2488457 to chronic spontaneous urticaria susceptibility, echoing the findings of this study regarding ITP. Both studies suggest that rs2488457 may not be a critical risk factor in certain immune-related conditions, prompting further research to identify other genetic variations that could better explain susceptibility. (Bufalo *et al.*, 2021) reported significant associations between the CC genotype of rs3789607 and Graves' disease susceptibility, contrasting with this study's focus on rs2488457 and its lack of significant findings in

Table 4: Correlation between *PTPN22* expression and rs2488457 genotype among acute and chronic cases with ITP.

Characteristics		rs2488457 genotyping			p-value
		Wild GG	Homo CC	Hetero GC	
<i>PTPN22</i> expression fold, median (range)	Acute	2.84 (2.84-2.84)	0.34 (0.01-1.95)	0.19 (0.01-2.52)	0.7965*
	Chronic	0.495 (0.04-0.95)	0.165 (0.01-3.41)	0.295 (0.11-2.69)	0.4313**

*p: Probability; Homo: Homozygous genotype; Hetero: Heterozygous genotype; *PTPN22*: Protein tyrosine phosphatase non-receptor type 22; * p-value represents variation among homo and hetero group as wild group has single value; ** p-value represents variation among homo and hetero group as wild group has two values.

Table 5: Correlations between BMI, age, hematological and serological parameters among acute cases with ITP.

Parameter	Age	BMI	Hb	WBC	PLT	ANA	IL-40	PA-Ab	<i>PTPN22</i>
Age		-0.72****	0.18	-0.33	0.23	-0.14	-0.07	0.04	-0.07
BMI	-0.72****		-0.12	0.40	-0.15	0.40	0.27	-0.01	0.11
Hb	0.18	-0.12		-0.06	0.08	-0.07	0.02	0.26	-0.05
WBC	-0.33	0.40	-0.06		0.02	-0.03	0.13	-0.07	0.19
PLT	0.23	-0.15	0.08	0.02		0.35	0.31	-0.22	-0.05
ANA	-0.14	0.40	-0.07	-0.03	0.35		0.63	0.55	-0.08
IL-40	-0.07	0.27	0.02	0.13	0.31	0.63		0.14	0.05
PA-Ab	0.04	-0.01	0.26	-0.07	-0.22	0.55	0.14		-0.15
<i>PTPN22</i>	-0.07	0.11	-0.05	0.19	-0.05	-0.08	0.05	-0.15	

*Numbers represent (r) value. Positive and negative r values represent positive and negative correlation respectively. R values of 0-0.3 (negligible), 0.3-0.5 (low), 0.5-0.7 (moderate), 0.7-0.9 (high) and 0.9-1 (very high) indicate level of correlation. *p*: probability; *P*-value of d-0.05 (*), d-0.01 (**), d-0.001 (***), d-0.0001 (****). BMI: Body mass index; *PTPN22*: Protein tyrosine phosphatase non-receptor type 22; ANA: Antinuclear Antibody; IL-40: Interleukin-40; PA-Ab: Anti-platelet antibody; PLT: Platelet; Hb: Hemoglobin; WBC: White blood cell.

ITP. This highlights the specificity of genetic markers in different autoimmune diseases, suggesting that while some SNPs may be important for one condition, they may not hold the same relevance for another. (Jabeen *et al.*, 2024) demonstrated a notable association between the CT genotype of rs2488457 and type 1 diabetes, with significant odds ratios. This study, however, found no significant differences in genotype frequencies among ITP patients. The differing results suggest that rs2488457 may play a more prominent role in type 1 diabetes than in ITP, emphasizing the need for condition-specific genetic investigations.

Zhang *et al.* (2025) found rs2488457 significantly associated with acute lymphoblastic leukemia progression-free survival, highlighting its potential importance in hematological malignancies. In contrast, this study reported no significant associations in ITP, which may indicate that while certain SNPs can influence disease outcomes in cancer, they may not have the same implications in autoimmune disorders like ITP, underscoring the diverse genetic landscape across diseases. (Su *et al.*, 2025). revealed a significant association between rs2476601 and an increased risk of type 1 diabetes, while this study found no significant associations for rs2488457 with ITP. This divergence emphasizes the possibility that different SNPs may have varying impacts on distinct autoimmune diseases, suggesting a complex interplay of genetic factors that warrants further exploration in the context of immune dysregulation.

CONCLUSION

As a whole, PA-Ab showed the most diagnostic promise in differentiating between acute and chronic ITP. The similar distribution of genotypes suggests that rs2488457 may not be associated with disease duration or progression from acute to chronic. The lack of significant variations suggests that rs2488457 genotype may not have a substantial impact on *PTPN22* expression levels in either acute or chronic individuals with ITP.

ACKNOWLEDGEMENT

Everyone who helped with this research, whether they were participants, physicians or guiders, is appreciated.

Funding

Self-funding.

Ethical clearance

The study proposal, outlining its objectives and methodologies, was submitted for ethical review to the Ethics Committee at the College of Science, University of Baghdad. Ethical clearance was granted under the reference number CSEC/0224/0021, dated 20 February 2024. The study adhered to the consent form guidelines as stipulated by the Iraqi Ministry of Health.

Conflict of interest

The authors declare that they have no conflicts of interest.

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