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Research Article

Assessment of the Relationship Between JAK2 V617F Mutation Status and Plasma Viscosity in Polycythemia Vera Patients

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Abstract

Objectives: Polycythemia vera (PV) is a chronic myeloproliferative neoplasm characterized by the clonal proliferation of myeloid cells with variable morphologic maturity and hematopoietic efficiency. In this study, we aimed to evaluate the association between plasma viscosity, a potential risk factor for thrombotic complications, and the *JAK2* V617F mutation.

Methods: Patients were classified into two subgroups: *JAK2* V617F mutation-positive and *JAK2* V617F-negative patients. A total of 60 patients were enrolled in the study, of whom 31 were *JAK2* V617F-positive and 29 were negative. In addition, we evaluated fibrinogen, albumin, erythrocyte sedimentation rate, and C-reactive protein (CRP) levels.

Results: Plasma viscosity values in *JAK2* V617F mutation-positive patients and *JAK2* V617F mutation-negative patients were found to be 1.089±0.126 mPa·s and 1.098±0.111 mPa·s, respectively (p=0.782). There was no relationship between plasma viscosity levels and the *JAK2* V617F mutation in polycythemia vera. In correlation analyses, fibrinogen was correlated with plasma viscosity in both groups (r=0.30, r=0.15). In addition, the erythrocyte sedimentation rate was correlated with plasma viscosity in both groups (r=0.230, r=0.272).

Conclusion: We were unable to demonstrate a relationship between plasma viscosity and the *JAK2* V617F mutation in patients with polycythemia vera. This study shows that plasma viscosity is affected by fibrinogen and other acute-phase reactants.

Keywords: Plasma viscosity, *JAK2* V617F, fibrinogen, erythrocyte sedimentation rate, polycythemia vera

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Polycythemia vera is a chronic myeloproliferative disease that leads to an uncontrolled increase in red blood cell count and increased blood viscosity, resulting in a predisposition to thrombosis.[1] It was first described in the late 19th century and is primarily caused by mutations in the *JAK2* gene. Epidemiologically, PV predominantly affects adults over 60 years of age, with a slightly higher incidence in males.[2] According to the 2022 World Health Organization (WHO) diagnostic criteria, it is classified as a BCR-ABL1–negative myeloproliferative neoplasm.[3] Hemoglobin levels greater than 16.5 g/dL for men and greater than 16 g/dL for women, along with evidence of increased

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cellularity in the erythroid lineage from a bone marrow biopsy and the presence of the *JAK2* V617F mutation, are recognized as key diagnostic criteria.[4]

The *JAK2* V617F mutation is crucial in PV as it leads to the constant activation of the JAK-STAT signaling pathway, which in turn encourages unchecked proliferation of hematopoietic cells.[5] Plasma viscosity, a measure of the blood's resistance to flow, is clinically relevant in PV, as elevated viscosity contributes to vascular complications and impaired microcirculation. Studies on blood viscosity in patients with polycythemia vera (PV) have shown elevated levels compared to healthy individuals, reflecting increased blood cell mass and altered plasma composition.[6]

A substitution of valine for phenylalanine at position 617 characterizes the *JAK2* V617F mutation, leading to the persistent stimulation of the JAK-STAT cascade. This mutation is found in approximately 95% of PV patients and is a key indicator for diagnosis.[7]

Plasma viscosity refers to the thickness and stickiness of plasma, which affects its flow properties in the circulatory system. It is typically measured using viscometers that assess the resistance of the plasma to flow under controlled conditions.[8]

In a subset of PV patients, the *JAK2* V617F mutation was absent. Our research involved measuring plasma viscosity in individuals diagnosed with PV based on the WHO 2008 criteria who lacked the *JAK2* V617F mutation, and these findings were compared to those of patients possessing the *JAK2* V617F mutation.

This study sought to elucidate the relationship between the existence of the *JAK2* V617F mutation and changes in plasma viscosity among patients diagnosed with PV. Understanding this relationship is crucial because plasma viscosity plays a significant role in the pathophysiology of PV and its associated thrombotic risks. By investigating these factors, this study seeks to contribute valuable insights that may improve the clinical management and prognostic assessment of PV cases.

Materials and Methods

Patients and Ethical Approval

Individuals diagnosed with PV according to the updated 2008 WHO diagnostic criteria at our outpatient clinic were included in the study. Since plasma viscosity could be affected by several conditions, the exclusion criteria were defined as a history of smoking, coronary artery disease, hyperlipidemia, peripheral arterial disease, oral contraceptive use, diabetes mellitus, and the presence of other malignancies.

Before participating in the study, all patients and their legally authorized representatives provided written informed consent. The duration since PV diagnosis was not considered during patient enrollment. The study involved 60 patients who were categorized into two groups based on whether they tested positive or negative for the *JAK2* V617F mutation. Plasma viscosity measurements obtained from both groups were compared.

The Ethics Committee of Ankara University Faculty of Medicine received the study protocol and granted approval on April 4, 2013, under decision number KA13/70 Approval Date 04/04/2013.

The viscosity of plasma was determined using a Brookfield DV-II+ cone-plate viscometer (Brookfield, Stoughton, MA, USA). To ensure sample homogeneity, fasting blood samples were obtained from each patient simultaneously in the morning. Anticoagulant tubes were utilized to collect 5 mL of whole blood samples, which were subsequently subjected to a 5-minute centrifugation process at 3,000 rpm. The plasma was then separated and stored at –40 °C. On the day of analysis, all samples were simultaneously thawed. Immediately before measurement, the samples underwent another round of centrifugation at 3,000 rpm for 2.5 minutes.

The viscosity of the plasma samples was measured at 37 °C using a viscometer calibrated with distilled water, according to a water viscosity value of 0.68 mPa·s. Alongside measuring plasma viscosity, evaluations were conducted on serum levels of C-reactive protein (CRP), fibrinogen, erythrocyte sedimentation rate (ESR), high-density lipoprotein (HDL), low-density lipoprotein (LDL), total protein, albumin, and complete blood count parameters. These parameters were compared between the two groups based on the status of the *JAK2* V617F mutation, and their effects on plasma viscosity were evaluated.

We identified the *JAK2* V617F mutation in our patients through the use of real-time polymerase chain reaction (PCR).

Statistical Analysis

Data analysis was conducted using the Statistical Package for the Social Sciences (SPSS) for Windows, Version 16.0 (IBM SPSS Inc., Chicago, IL, USA). In the descriptive statistics, categorical variables were represented as counts and percentages, continuous variables with a normal distribution were shown as mean ± standard deviation, and those without a normal distribution were described using median and range values.

To evaluate pairs of data, the independent samples t-test was utilized for parametric distributions, whereas the Mann–Whitney U test was employed for non-parametric ones. In terms

of correlation analysis, Pearson's correlation coefficients were applied to parametric variables, while Spearman's correlation coefficients were used for non-parametric variables.

Results

Demographic Findings

This study involved 60 individuals who had been diagnosed with PV. The *JAK2* V617F mutation was positive in 31 patients and negative in 29 patients. The overall mean age of the patients was 57±17.9 years. The mean age was 70±10.6 years in the *JAK2* V617F mutation–positive group and 44±14.3 years in the *JAK2* V617F mutation–negative group (p<0.001).

In terms of gender distribution, there were 24 female patients, accounting for 40%, and 36 male patients, making up 60%. Among those with the *JAK2* V617F mutation, 19 out of 31 patients were female, representing 59%, while 12 were male, comprising 41%. Conversely, in the group without the *JAK2* V617F mutation, 24 of the 29 patients were male, which is 87%, and 5 were female, equating to 13% (Table 1).

Table 1. Patients age, sex and cytoreductive therapy status

	JAK2 V61F(+) n=31	JAK2 V617F(-) n=29
Sex (M/F)	12 (39%)/19 (61%)	24 (83%)/5 (17%)
Age (Years)	70±10.63	44.3±14.3
Cytoreductive therapy (receiving/not receiving)	27 (87.1%) / 4 (12.9%)	1 (3.4%)/28 (96.6%)

The number of patients who received cytoreductive therapy for PV was 28 (46.7%), while 32 (53.3%) did not. In the *JAK2* V617F mutation–positive group, 27 of 31 patients (87.1%) were receiving treatment. In contrast, only one of 29 patients (3.4%) in the *JAK2* V617F mutation–negative group was receiving treatment (p<0.001). Among the 28 patients receiving cytoreductive therapy, hydroxyurea was used in 22 patients, anagrelide in 4 patients, and hydroxyurea plus anagrelide in 2 patients.

Plasma Viscosity and Other Parameters

In our research, we utilized an independent samples t-test to compare plasma viscosity measurements between the two groups. The mean plasma viscosity was 1.089±0.12 mPa·s in the *JAK2* V617F mutation–positive group and 1.098±0.11 mPa·s in the *JAK2* V617F mutation–negative group. The two groups did not show any statistically significant differences (p=0.782) (Fig. 1).

Comparison of fibrinogen levels, which are known to affect plasma viscosity, revealed no significant differences between the groups (p=0.091). In the group without the *JAK2* V617F mutation, total protein levels were notably elevated (p=0.022). However, there was no statistically significant difference in albumin levels between the groups (p=0.078). Similarly, HDL and LDL levels did not show significant differences between the two groups (HDL:p=0.520; LDL:p=0.276). The difference in erythrocyte sedimentation rate (ESR) was also not statistically significant (p=0.382). However, in the group with the *JAK2* V617F mutation, C-reactive protein (CRP) levels were notably elevated (p=0.014).

Table 2. Laboratory results according to JAK2 V617F status

Parameters	JAK2 V617F (+)	JAK2 V617F (–)	p	Reference range
Plasma viscosity (mPa·s)	1.089±0.126	1.098±0.111	0.782	1.15–1.35 mPa·s
Hemoglobin (g/dL)	15.8±2.58	17.83±1.34	**0.001**	12–16 g/dL
Hematocrit (%)	48.5±7.64	53.4±3.38	**0.002**	34–45%
Leukocyte count (/µL)	11.160±5.660	9.260±3.110	0.117	4,000–10,000 /µL
Platelet count (/µL)	401.900±20.100	304.000±11.190	**0.025**	150,000–400,000 /µL
C-reactive protein (CRP) (mg/L)	5.5±1.16	2.37±0.35	**0.014**	0–5 mg/L
Fibrinogen (mg/dL)	327±77	296±62	0.091	190–400 mg/dL
High-density lipoprotein (HDL) (mg/dL)	45.1±8.3	46.6±9.9	0.520	40–60 mg/dL
Low-density lipoprotein (LDL) (mg/dL)	101±26.1	108±27.1	0.276	55–160 mg/dL
Total protein (g/dL)	7.16±0.50	7.41±0.30	**0.022**	6.0–8.7 g/dL
Albumin (g/dL)	4.02±1.20	4.10±0.89	0.078	3.5–5.0 g/dL
Erythropoietin (mIU/mL)	2.08±1.48	2.98±1.47	**0.022**	5–16 mIU/mL
Erythrocyte sedimentation rate (ESR) (mm/h)	8.41±6.60	6.92±6.37	0.382	0–20 mm/h

ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; HDL: High-density lipoprotein; LDL: Low-density lipoprotein.

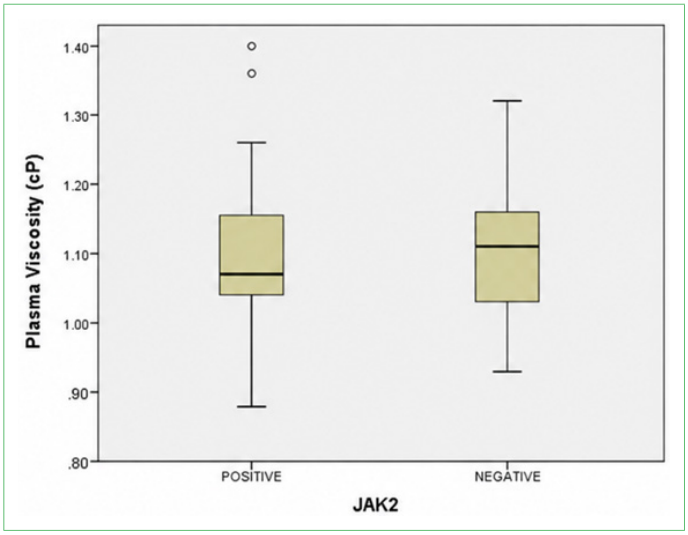

Figure 1. Comparison of plasma viscosity levels according to JAK2 V617F mutation status (p=0.782).

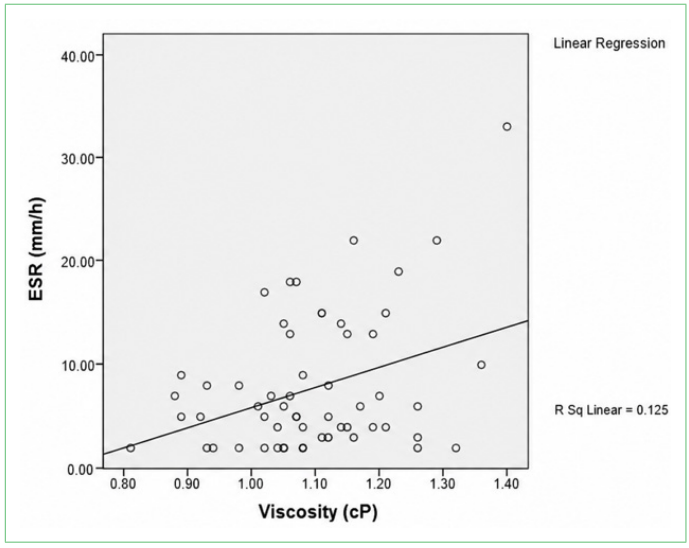

Figure 2. Positive correlation between ESR values and plasma viscosity in both groups (r=0.219).

In the group with the *JAK2* V617F mutation, erythropoietin (EPO) levels were notably lower compared to the group without the mutation (p=0.022) (Table 2).

Hemoglobin and hematocrit levels were higher in the mutation–negative group. However, the number of patients receiving cytoreductive therapy was significantly higher in the mutation-positive group (p<0.001). No significant difference was observed in leukocyte counts between the two groups (p=0.117). In contrast, the group with the mutation exhibited a notably increased platelet count (p=0.025). EPO measurements were lower in the *JAK2* V617F-positive group than the negative group (p=0.022).

In our study, the correlations between plasma proteins, CRP, ESR values, and plasma viscosity were evaluated (Fig. 2). Correlation analyses were performed between plasma viscosity and the variables within each group, and the relationships were assessed according to the correlation coefficient (r).

Fibrinogen levels were moderately correlated with plasma viscosity in the mutation-positive group (r=0.30). In the mutation-negative group, the correlation with plasma viscosity was weaker (r=0.150). ESR values were moderately correlated with plasma viscosity in both groups (r=0.23 and r=0.272, respectively).

There was no notable relationship found between LDL and HDL levels and plasma viscosity in either group (for LDL:r=-0.115 and r=0.02, respectively; for HDL:r=0.08 and r=-0.170, respectively). Total protein levels in the mutation-positive group indicated a moderate correlation with plasma viscosity (r=0.293). Similarly, albumin levels in the mutation-positive group were moderately correlated with

Table 3. Correlation of variables with plasma viscosity according to JAK2 V617F mutation status

Variables	JAK2 V617F (+)		JAK2 V617F (-)	
	r	p	r	p
Parametric variables				
HDL	0.08	0.968	-0.170	0.328
Fibrinogen	**0.30**	0.876	0.150	0.437
Total Protein	**0.293**	0.115	0.122	0.528
Albumin	**0.236**	0.135	0.132	0.456
Non-parametric variables				
CRP	-0.170	0.368	0.095	0.311
LDL	-0.115	0.262	0.120	0.533
ESR	**0.230**	0.903	**0.272**	0.153

ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; HDL: High-density lipoprotein; LDL: Low-density lipoprotein.

plasma viscosity (r=0.236) (Table 3). CRP levels demonstrated only a weak correlation with plasma viscosity in both groups (r=0.170 and r=0.095).

Discussion

It is well established that whole blood viscosity is increased in patients with PV, and this increase is associated with a higher incidence of thromboembolic complications. Unlike whole blood viscosity, plasma viscosity is not affected by parameters such as hematocrit, hemoglobin, leukocyte count, or platelet count. In contrast, plasma viscosity is more closely associated with inflammation and elevated plasma protein levels.[9]

Increased plasma viscosity is considered an important predictor of cardiovascular events in patients with hyperviscosity syndrome.[10] Elevated blood viscosity predominantly leads to stasis within the capillary beds and veins, characterized by a low blood flow velocity.

The *JAK2* V617F mutation negatively impacts the outlook for patients with PV. In a study conducted by Vannucchi et al.[11] involving 173 PV patients, *JAK2* V617F mutation positivity was associated with increased hematocrit and leukocyte counts, whereas platelet counts were decreased. However, approximately 5–10% of patients diagnosed with PV do not harbor this mutation after secondary causes of polycythemia have been excluded from consideration. Our study aimed to explore whether there is a difference in plasma viscosity between individuals with the *JAK2* V617F mutation and those without it, as the current literature offers limited data on this topic.

Our research found that the *JAK2* V617F mutation did not correlate with higher plasma viscosity when compared to patients without the mutation. Nevertheless, *JAK2* mutation positivity is associated with increased whole blood viscosity. In a meta-analysis published in 2024 by Chen et al.[12], patients harboring this mutation, particularly those with a high mutant allele burden, were found to have an increased risk of thrombosis, splenomegaly, myelofibrosis, and acute myeloid leukemia. Although our findings demonstrated no effect of mutation positivity on plasma viscosity, the clinical differences observed in mutation-positive patients are more likely attributable to increased whole blood viscosity.

Although we did not demonstrate an increase in plasma viscosity according to the *JAK2* V617F mutation status, other biochemical markers known to affect plasma viscosity were also evaluated in this study. One of these parameters is fibrinogen. The groups did not show any notable differences in fibrinogen levels. However, a positive relationship between fibrinogen and plasma viscosity was demonstrated. Similarly, erythrocyte sedimentation rate (ESR) values were evaluated, and no significant differences were found between the groups. Nevertheless, similar to fibrinogen, ESR demonstrated a positive correlation with plasma viscosity. These findings are consistent with previously established knowledge. Based on these results, it may be suggested that plasma viscosity is influenced more by acute-phase reactants such as fibrinogen and ESR rather than by the mutation status. Fibrinogen is known to increase erythrocyte aggregation and plasma viscosity.[13] Therefore, rather than mutation positivity alone, conditions associated with elevated plasma protein levels, such as chronic infections, smoking, and hypercholesterolemia, should be more carefully managed and treated in this patient population.

We also evaluated the complete blood count parameters in our study. The group with the mutation had lower hematocrit levels compared to the group without the mutation. Platelet counts were lower in the mutation-positive group. Under normal circumstances, patients with *JAK2* V617F mutation positivity are expected to exhibit higher hematocrit levels, and the mutant allele burden is known to play an important role in this association.[14] Therefore, these findings were not unexpected in our study, since 87% of mutation-positive patients had received cytoreductive therapy for PV, whereas this rate was only 3.4% among the mutation-negative patients. Most mutation-negative patients were primarily managed with phlebotomy alone.

Our study has some limitations. The study included patients who were diagnosed based on the 2008 WHO guidelines, which were valid at the time of the study. Currently, the 2022 WHO criteria are used for the diagnosis of PV, and bone marrow biopsy is considered a major diagnostic criterion. In patients diagnosed during the study period, secondary causes of polycythemia were excluded as thoroughly as possible from the study. In particular, erythropoietin levels were given greater consideration when establishing the diagnosis in mutation-negative patients. Although the current literature investigating the relationship between mutation positivity and plasma viscosity remains limited, it should also be noted that this study was conducted several years ago.

Conclusion

In conclusion, plasma viscosity did not vary according to the presence of the *JAK2* V617F mutation in our study. Although whole blood viscosity is known to increase in patients with PV, particularly in the presence of the *JAK2* V617F mutation due to erythroid lineage expansion, no significant alterations in plasma viscosity were observed. Plasma viscosity is predominantly influenced by plasma proteins and acute-phase reactants. Therefore, in this pa-

tient population, which already exhibits increased whole blood viscosity, factors that may promote inflammation and elevate acute-phase reactants should be avoided in treatment.

This research focused on examining the connection between the *JAK2* V617F mutation and plasma viscosity in individuals with PV. Plasma viscosity showed no correlation with the presence of *JAK2* V617F positivity. An increase in acute-phase reactants results in increased plasma viscosity. Elevations in ESR and fibrinogen levels lead to an increase in plasma viscosity. Plasma viscosity can act as an acute-phase reactant and serves as a significant risk factor for thrombotic events in patients with PV. During PV, conditions such as infection, inflammation, tissue injury, burns, and trauma may facilitate the development of thrombotic events.

Disclosures

Ethics Commitee Approval: The Ethics Committee of Ankara University Faculty of Medicine received the study protocol and granted approval on April 4, 2013, under decision number KA13/70 Approval Date 04/04/2013.

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References

1. Tefferi A, Barbui T. Polycythemia vera: 2024 update on diagnosis, risk-stratification, and management. Am J Hematol 2023;98(9):1465–87. [CrossRef]
2. Maffioli M, Mora B, Passamonti F. Polycythemia vera: from new, modified diagnostic criteria to new therapeutic approaches. Clin Adv Hematol Oncol 2017;15(9):700–7.
3. Mroczkowska-Bękarciak A, Wróbel T. BCR::ABL1-negative myeloproliferative neoplasms in the era of next-generation sequencing. Front Genet 2023 ;14:1241912. [CrossRef]
4. Lee N, Erdos K, Scandura JM, Abu-Zeinah G. Importance of Diagnosing Polycythemia Vera (PV) Patients (pts) whose hematocrit (HCT)/hemoglobin (HGB) are less than the who 2022 stipulated criteria. Blood 2023;142:6434. [CrossRef]
5. Means RT. JAK2 V617F and the evolving paradigm of polycythemia vera. Korean J Hematol 2010;45(2):90–4. [CrossRef]
6. Shin DW, Gu JY, Kim JS, Jung JS, Shin DY, Koh Y, et al. Increased plasma viscosity in plasma cell dyscrasia and whole blood viscosity in polycythemia vera. Clin Hemorheol Microcirc 2018;70(1):59–67. [CrossRef]
7. Bellosillo B, Michael Doubek, Tomuleasa C, Griesshammer M, Marchetti M, Sacha T, et al. JAK2 mutations in polycythemia vera: from molecular origins to inflammatory pathways and clinical implications. Magazine Eur Med Oncol 2025;17(Suppl 4):79–93. [CrossRef]
8. Vizza P, Tradigo G, Parrilla M, Guzzi PH, Gnasso A, Veltri P. On blood viscosity and its correlation with other biological parameters. International Conference on Computational Science. Berlin/Heidelberg: Springer; 2018. [CrossRef]
9. Baskurt O. Rheologic properties of blood. Doğa Tr J Med Sci 1990;14:433-437.
10. Yamagishi M, Yasumura, YK, Bando K. A giant aneurysm in coronary-pulmonary artery fistula associated with mural thrombus. Heart 2000;84(4):364. [CrossRef]
11. Vannucchi AM, Antonioli E, Guglielmelli P, Longo G, Pancrazzi A, Ponziani V, et al; MPD Research Consortium. Prospective identification of high-risk polycythemia vera patients based on JAK2(V617F) allele burden. Leukemia 2007;21(9):1952–9. [CrossRef]
12. Chen CC, Chen JL, Lin AJ, Yu LH, Hou HA. Association of JAK2V617F allele burden and clinical correlates in polycythemia vera: a systematic review and meta-analysis. Ann Hematol 2024;103(6):1947–65. [CrossRef]
13. Rasyid A, Harris S, Kurniawan M, Mesiano T, Hidayat R. Fibrinogen and LDL influence on blood viscosity and outcome of acute ischemic stroke patients in Indonesia. Ann Neurosci 2019;26(3-4):30–4. [CrossRef]
14. Lee AJ, Kim SG, Nam JY, Yun J, Ryoo HM, Bae SH. Clinical features and outcomes of JAK2 V617F-positive polycythemia vera and essential thrombocythemia according to the JAK2 V617F allele burden. Blood Res 2021;56(4):259–65. [CrossRef]