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The clinical characteristics of Janus Kinase 2-positive myeloproliferative neoplasms in Saudi Arabia

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Abstract:

BACKGROUND: Janus kinase 2 (JAK2) mutation is a major genetic aberration in 95% of patients with polycythemia vera (PV) and approximately 50% in those with essential thrombocythemia (ET). Previous studies have reported inconsistent findings regarding the effects of JAK2 mutations in myeloproliferative neoplasms (MPNs).

OBJECTIVES: This study investigated the influence of JAK2 mutations on the clinical characteristics of MPNs in Saudi Arabia.

MATERIALS AND METHODS: This retrospective study analyzed the clinical profiles of 71 Saudi patients diagnosed with JAK2-positive MPNs (28 PV and 43 ET) between 2021 and 2024. Data were collected from a laboratory database and stratified by disease subtype, gender, and risk category. Statistical analyses were performed to identify the differences in clinical features and outcomes.

RESULTS: The mean age of the participants was 54 years, with no significant age difference between the PV and ET groups. The PV group was mostly male, while the ET group was mostly female. This study found that the rates of thrombosis, major hemorrhage, leukocytosis, polycythemia, and thrombocytosis in PV and ET were consistent with previous research. However, the mean leukocyte counts and proportion of patients with high-risk scores were significantly higher in the PV group than in the ET group. In addition, the mean platelet count with ET was significantly higher in female patients; however, the proportion of male ET patients with high-risk scores was higher.

CONCLUSIONS: The research findings are consistent with prior studies and shed further light on the impact of JAK2 mutations on the clinical characteristics of MPNs.

Keywords:

Essential thrombocythemia, Janus kinase 2 mutation, myeloproliferative neoplasms, polycythemia vera

Introduction

Myeloproliferative neoplasms (MPNs) are a diverse set of clonal disorders that affect hematopoietic stem cells, marked by the overproduction of both mature and immature blood cells originating from myeloid lineages.[1,2] Clinically, these disorders are associated with an elevated risk of thrombosis and hemorrhage, along with the potential to progress to marrow fibrosis, myelodysplastic syndrome, or acute myeloid leukemia.[3] According to the World Health Organization (WHO) classification criteria for 2016 and 2022, polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF) are the most common categories of Philadelphia-negative (Ph-negative) MPNs.[4,5] The diagnostic criteria for MPNs include a correlation between clinical characteristics, pathological evaluation of bone marrow biopsy, and the molecular landscape.

The most significant somatic mutations in MPNs include mutations in exon 14

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of Janus Kinase 2 (JAK2 V617F), exon 12 of JAK2, myeloproliferative leukemia virus oncogene exon 10 (MPL515), and calreticulin exon 9 (CALR). These genetic alterations contribute to the dysregulation of hematopoiesis and the subsequent overproduction of blood cells in MPNs. Identification of these mutations not only provides valuable insights into the molecular mechanisms driving MPNs, but also improves diagnostic approaches and facilitates the development of targeted therapies for managing these disorders.[6] In 2005, the discovery of the JAK2 V617F mutation marked the first recurrent molecular abnormality in Ph-negative MPNs, offering critical insight into their genetic underpinnings.[7,8] This mutation, found in 95% of PV and 50% of ET/PMF patients, enhances the sensitivity of hematopoietic cells to growth factors such as erythropoietin and thrombopoietin, thereby promoting the proliferation of myeloid cell lines.[9] The WHO has included JAK2 mutation as one of the major diagnostic criteria for MPNs.[4,5]

Further investigations revealed that 2%–5% of JAK2 V617F-negative PV cases exhibited mutations in JAK2 exon 12 and 10% of patients with JAK2 V617F-negative ET or PMF with mutations in MPL515.[10-12] In 2013, somatic mutations in the CALR gene were identified in the majority of ET or PMF patients lacking JAK2 or MPL515 mutations.[13] Several international studies have reported inconsistent findings regarding the effect of the JAK2 V617F mutation on the clinical profile and overall survival (OS) of patients with MPN.[3,14-22] Despite extensive international studies on the effect of the JAK2V617F mutation on the clinical profile of patients with MPN, regional studies exploring this effect in Saudi Arabian patients remain scarce. This study aims to address this gap by describing the impact of JAK2 mutations on the clinical characteristics of MPNs in a cohort of Saudi Arabian patients.

Materials and Methods

Study population and design

This retrospective study assessed the clinical manifestations, laboratory findings, and management approaches of a cohort of Saudi Arabian patients with JAK2-positive MPNs treated at Dr. Sulaiman Al-Habib Hospital between 2021 and 2024. Data were collected from the laboratory records of patients who were screened for unusual site thrombosis or clinically suspected of having MPNs. The study included all patients who met the 2016 WHO diagnostic criteria for JAK2-positive and Ph-negative MPNs.[4] The patients were subsequently stratified into low- and high-risk categories based on the prognosis and therapeutic management.[23]

Patients with secondary erythrocytosis and thrombocytosis, infection-related leukocytosis, or marrow fibrosis unrelated to myelofibrosis were excluded from the study. In addition, patients who lacked documented clinical manifestations and laboratory investigations were excluded.

At the time of diagnosis, both clinical and laboratory information was gathered from all participants. This included age, gender, and cardiac risk factors. We also recorded the presence of organomegaly, a history of arterial and venous thromboembolism (VTE), total leukocyte count (TLC), hemoglobin levels (Hb), hematocrit (HCT), and platelet count (PLT). Furthermore, we outlined the management approach, which may include initiation cytoreductive therapy (e.g., hydroxyurea) or the use of antiplatelet or anticoagulant treatments.

Method of molecular genetic analysis of the Janus kinase 2 p.(V617F) mutation

Genomic DNA (gDNA) was examined for the JAK2 V617F mutation with real-time polymerase chain reaction (real-time PCR) using a MutaScreen Kit (Qiagen, Hilden, Germany; detection threshold: 2%). The c. 1849G>T p.(V617F) variant in exon 14 of JAK2 (OMIM 147796; chromosome 9p24.1) was assessed according to the manufacturer's instructions. gDNA extraction and analysis involved several steps: (1) gDNA was extracted from peripheral blood using standard DNA extraction methods (silica-based column purification). (2) The extracted gDNA was quantified at 260 nm, and its purity was assessed using spectrophotometry (NanoDrop). (3) The MutaScreen Kit included primers and probes for the JAK2 V617F mutation. Real-time PCR was performed by mixing gDNA with reagents, including mutation-specific primers, probes, and a master mix containing DNA polymerase, deoxynucleoside triphosphates (dNTPs), and buffer components. (4) PCR was performed using a real-time system. The reaction involved initial denaturation, followed by cycles of denaturation, annealing, and extension. The fluorescence from the probes was measured in real time to detect and quantify the JAK2 V617F mutation. (5) The PCR instrument software analyzed the fluorescence data to determine the presence and quantity of the mutation.

Statistical analysis

Data collection and evaluation were conducted using an Excel spreadsheet, along with the Statistical Package for the Social Sciences (SPSS) (version 20, IBM Corp., Armonk, NY, USA). Statistical significance was defined as $P < 0.05$, with a 95% confidence interval. The findings were expressed as mean, standard deviation, or median (range).

Ethical approval

The Institutional Review Board of the Al-Habib Research Center in Saudi Arabia granted approval

for the study (reference number RC24.09.82). Patient confidentiality was strictly maintained, and a waiver of consent was granted due to the use of fully anonymized data, as it would not pose any risk to the participants. All procedures adhered to the ethical standards outlined in the Declaration of Helsinki, as well as the guidelines established by both the institution and the National Research Council in Saudi Arabia.

Results

This study included 71 Saudi Arabian patients diagnosed with JAK2-positive MPNs. The cohort included 34 females (47.88%) and 37 males (52.11%), with 28 patients (39.43%) having PV and 43 patients (60.56%) having ET. The mean age of all participants was 54 ± 17.7 years, with the PV group being older than the ET group; however, the difference was not significant (P = 0.451952). The gender distribution varied between the PV and ET groups, showing a predominance of males in the PV group and females in the ET group (P = 0.0085).

No significant differences were observed between male and female participants or between PV and ET patients in terms of mean age, incidence of splenomegaly, arterial thrombosis, VTE, major hemorrhage, smoking, cardiovascular (CV) disease risk factors, use of cytoreductive therapy, antiplatelet therapy, and anticoagulant use. However, the proportion of patients with high-risk scores and mean TLC was significantly higher in the PV group than in the ET group ($P < 0.05$). In addition, in patients with PV and ET, the mean Hb and HCT levels were notably higher in males than in females ($P < 0.05$). Moreover, the mean PLT with ET was significantly higher in female patients; however, the proportion of male ET patients with high-risk scores was higher ($P < 0.05$). Table 1 summarizes the data for patients with JAK2-positive MPN. Tables 2 and 3 summarize the gender distribution data of patients with JAK2-positive PV and ET.

Table 1: Comprehensive data for patients with Janus kinase 2-positive, myeloproliferative neoplasms

Parameters	MPN (*n*=71), *n* (%)	PV (*n*=28), *n* (%)	ET (*n*=43), *n* (%)	*P*
Age (years)*	54±17.7	56±13.6	53±20	0.451952
Males	37 (52.11)	20 (71.4)	17 (39.5)	0.0085
Females	34 (47.88)	8 (28.6)	26 (60.5)	0.0085
TLC (mm^3)*	9±3.7	10±4.3	8±3	0.031981
Hb (g/dL)*	16±2.9	18±1.8	14.5±1.9	0.0145
HCT (%)*	49±9.1	56±5.6	45±7.1	0.0235
PLT (mm^3)*	640±266	483±230	753±223	0.000001
Splenomegaly	11 (15.49)	6 (21.42)	5 (11.62)	0.3228
Arterially thrombosis	12 (16.9)	4 (14.28)	8 (18.6)	0.7526
VTE	8 (11.26)	4 (14.28)	4 (9.3)	0.7036
Major hemorrhage	2 (2.81)	2 (7.14)	0	0.1521
Smoking	12 (16.9)	8 (28.5)	4 (9.3)	0.0514
Risk factors for CVDs	34 (47.88)	16 (57)	18 (41.8)	0.2102
Cytoreductive therapy	44 (61.97)	20 (71.42)	24 (55.81)	0.1855
Anti-platelet	66 (92.95)	27 (96.42)	39 (90.69)	0.3567
Anticoagulant	9 (12.67)	4 (14.28)	5 (11.62)	0.7318
High risk score	50 (70.42)	23 (82.14)	17 (39.53)	0.0004

*The data were given as a mean±SD, The comparison of the mean values was made with *Z*-test, *P*<0.05. TLC=Total leukocyte count, Hb=Hemoglobin, HCT=Hematocrit, PLT=Platelet, VTE=Venous thromboembolism, CVDs=Cardiovascular diseases, PV=Polycythemia vera, ET=Essential thrombocythemia, SD=Standard deviation, MPN=Myeloproliferative neoplasm

Discussion

This study describes the clinical features of 71 Saudi Arabian patients with JAK2-positive MPNs (28 PV and 43 ET). Previous studies have indicated that JAK2-positive MPNs are more prevalent in adulthood.[24] Accordingly, the mean age of all participants in this study was above 50 years, with the PV group being older than the ET group; however, the difference was not significant. The higher mean age in the PV group compared to the ET group can be attributed to factors such as the higher prevalence and allele burden of the JAK2V617F mutation and increased JAK2V617F homozygosity in older PV patients.[25,26] The median age of patients diagnosed with PV was 56 years, and 14% of the patients were younger than 40 years, aligning with earlier literature findings.[27] The present study determined that patients diagnosed with ET had a median age of 53 years, with an age range of 19–90 years. This observation supports the findings of the Mayo-Florence study, which included 2000 patients with ET.[28,29]

In addition, the findings of study project corroborate previous research findings indicating an unequal sex distribution between the PV and ET groups, with more males in the PV group and more females in the ET group.[19,30] This result may be explained by several factors related to the JAK2V617F mutation and its interaction with sex-specific biological mechanisms. The higher prevalence of JAK2V617F homozygous-mutant precursors in PV correlates with more pronounced hematological abnormalities at the time of diagnosis. This homozygous mutation occurs more frequently in males, which may explain the higher incidence of PV observed in the male population. Moreover, the phenotypic effects of JAK2V617F homozygosity are influenced by both age and sex, with male patients with PV exhibiting a greater number of homozygous-mutant colonies.[31] In contrast to PV, the JAK2V617F mutation in ET is less often homozygous and is influenced by additional genetic or epigenetic elements. Studies have shown that estrogen facilitates megakaryocyte polyploidization through estrogen receptor beta-mediated GATA1 transcription, potentially explaining the higher incidence of ET among women. This mechanism could clarify the female

Table 2: Gender distribution data for patients with Janus Kinase 2-positive polycythemia vera (polycythemia vera)

Parameters	Total (*n*=28), *n* (%)	Males (*n*=20; 71.4), *n* (%)	Females (*n*=8; 28.6), *n* (%)	*P*
Age (years)*	56±13.6	57±13.5	54±14.4	0.612255
TLC (mm3)*	10±4.3	11±4.6	9±3.6	0.051748
Hb (g/dL)*	18±1.8	19±1.8	17±1.5	0.000001
HCT (%)*	56±5.6	58±5.6	53±4	0.000043
PLT (mm3)*	483±230	488±233	472±239	0.779543
Splenomegaly	6 (21.4)	6 (10)	0	0.1412
Arterially thrombosis	4 (14.3)	4 (20)	0	0.2947
VTE	4 (14.3)	3 (15)	1 (12.5)	1.00
Major hemorrhage	2 (7)	2 (10)	0	1.00
Smoking	8 (28.5)	8 (40)	0	0.0628
Risk factors for CVDs	16 (57)	13 (65)	3 (37.5)	0.2309
Cytoreductive therapy	20 (71.4)	15 (75)	5 (62.5)	0.6508
Anti-platelet	27 (96.4)	19 (95)	8 (100)	0.5195
Anticoagulant	4 (14.3)	3 (15)	1 (12.5)	0.31731
High risk score	23 (82.1)	18 (90)	5 (62.5)	0.1231

*The data were given as a mean±SD, The comparison of the mean values was made with *Z*-test, *P*<0.05. TLC=Total leukocyte count, Hb=Hemoglobin, HCT=Hematocrit, PLT=Platelet, VTE=Venous thromboembolism, CVDs=Cardiovascular diseases, SD=Standard deviation

Table 3: Gender distribution data for patients with Janus Kinase 2-positive essential thrombocythemia (essential thrombocythemia)

Parameters	Total (*n*=43), *n* (%)	Males (*n*=17; 39.5), *n* (%)	Females (*n*=26; 60.5), *n* (%)	*P*
Age (years)*	53±20	53±18	52±21.4	0.868841
TLC (mm3)*	8±3	7±2.9	8±2.8	0.262429
Hb (g/dL)*	14.5±1.9	15.9±1.3	13.7±1.7	0.000002
HCT (%)*	45±7.1	50±6.5	42±5.6	0.000031
PLT (mm3)*	753±223	654±168	818±233	0.007390
Splenomegaly	5 (11.6)	1 (5.8)	4 (15.3)	0.6327
Arterially thrombosis	8 (18.6)	3 (17.6)	5 (19.2)	1.00
VTE	4 (9.3)	0	4 (15.3)	0.1404
Major hemorrhage	0	0	0	1.00
Smoking	4 (9.3)	3 (17.6)	1 (3.8)	0.2837
Risk factors for CVDs	18 (41.8)	8 (47)	10 (38.4)	0.5761
Cytoreductive therapy	24 (55.8)	8 (47)	16 (61.5)	0.3493
Anti-platelet	39 (90.7)	37 (100)	22 (84.6)	0.0893
Anticoagulant	5 (11.6)	0	5 (19.2)	0.1390
High risk score	17 (39.5.1)	11 (64.7)	6 (23)	0.0062

*The data were given as a mean±SD, The comparison of the mean values was made with *Z*-test, *P*<0.05. TLC=Total leukocyte count, Hb=Hemoglobin, HCT=Hematocrit, PLT=Platelet, VTE=Venous thromboembolism, CVDs=Cardiovascular diseases, SD=Standard deviation

preponderance in ET, as women typically have elevated estrogen levels that affect megakaryocyte differentiation and platelet generation.[32]

Patients diagnosed with MPNs are more likely to experience thrombotic and hemorrhagic events. The underlying mechanisms of the hypercoagulable state are primarily attributed to elevated blood viscosity, along with increased platelet and leukocyte counts, which collectively contribute to dysregulated hemostasis.[33] It is important to highlight that patients with a PLT $\geq 1000 \times 10^9$/L may experience bleeding due to acquired Von Willebrand disease, particularly when receiving antiplatelet therapy. Assessing the risk of thrombosis and bleeding is crucial for the proper stratification of MPNs and for determining the most suitable treatment approach.

In terms of clinical symptoms, 12% of patients with ET had splenomegaly, which is consistent with the existing literature.[28,29] However, this study revealed a significantly lower prevalence of splenomegaly (21%) in patients with PV than the 36% reported by Tefferi *et al*.[27] The incidence rates of thrombosis (ranging from 8% to 22%) and major hemorrhage (between 4% and 8%) for PV and ET in our study were consistent with previously reported findings.[27-29]

Notably, this study revealed that the PV group exhibited higher mean leukocyte counts and elevated high-risk scores than the ET group. In assessing the prognostic risk for MPN, considerations include advanced age, a previous history of thrombosis, and leukocytosis. The study found that participants in the PV group were,

on average, older than those in the ET group. The JAK2V617F mutation is found in virtually all PV cases and is associated with a higher risk of thrombosis. The JAK2V617F mutation occurs in half of ET patients, while other mutations, such as CALR and MPL, are associated with distinct clinical manifestations and lower leukocytosis rates.[34]

In our cohort, 35% of patients with PV had leukocytosis at diagnosis, and 46% had thrombocytosis, which is consistent with the data from Tefferi *et al*.[27] In addition, 23% of ET patients presented with leukocytosis, 35% with erythrocytosis, and 16% with extreme thrombocytosis (PLT $\geq 1000 \times 10^9$/L). This corroborates the findings of the Mayo-Florence study, which included 2000 patients with ET.[28,29] However, we observed a lower percentage of (42%) ET patients who had CV risk factors compared to the Mayo-Florence study findings (54%–52%).

The findings of this study indicate that women with ET exhibit a significantly higher mean PLT than men. This observed difference may be influenced by several factors, including hormonal variations and compensatory mechanisms associated with menstrual blood loss, both of which play a role in platelet production and regulation. Furthermore, the higher rate of clonal hematopoiesis among female patients with ET may also contribute to elevated PLTs.[35,36] This study found that male ET patients exhibited a significantly higher rate of high-risk scores than female patients ($P < 0.05$). The higher incidence of thrombotic events and reduced OS in males can be attributed to several factors. First, male gender was initially identified as an independent variable associated with an increased risk of thrombosis in patients with ET. Second, male ET patients tend to exhibit higher leukocyte counts and more frequent JAK2V617F mutations, both of which are recognized as the factors that increase the risk of thrombosis. These sex-specific characteristics account for the disparities in thrombotic events and survival outcomes between male and female ET patients.[37,38]

This study has certain limitations that should be acknowledged. First, the sample size was relatively small compared to that used by Tefferi *et al*., which may have affected the generalizability of the findings. Second, the retrospective nature of the study introduces the potential for bias, underscoring the necessity for future prospective investigations to validate our results and strengthen the comparative analyses.

Conclusions

This study aimed to assess the impact of JAK2 mutations on the clinical profile of MPNs in Saudi Arabia. Our findings are consistent with previous observations and provide further insights into the role of JAK2 mutations in shaping the clinical characteristics of MPNs. Future prospective studies are essential for validating these results and enhancing comparative analyses.

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Conflicts of interest

There are no conflicts of interest.

References

1. Tefferi A, Barbui T. Polycythemia vera: 2024 update on diagnosis, risk-stratification, and management. Am J Hematol 2023;98:1465-87.
2. Tefferi A, Vannucchi AM, Barbui T. Essential thrombocythemia: 2024 update on diagnosis, risk stratification, and management. Am J Hematol 2024;99:697-718.
3. Almedal H, Vorland M, Aarsand AK, Grønningsæter IS, Bruserud Ø, Reikvam H. Myeloproliferative neoplasms and JAK2 mutations. Tidsskr Nor Laegeforen 2016;136:1889-94.
4. Arber DA, Orazi A, Hasserjian R, Thiele J, Borowitz MJ, Le Beau MM, *et al*. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood 2016;127:2391-405.
5. Khoury JD, Solary E, Abla O, Akkari Y, Alaggio R, Apperley JF, *et al*. The 5th edition of the World Health Organization classification of haematolymphoid tumours: Myeloid and histiocytic/dendritic neoplasms. Leukemia 2022;36:1703-19.
6. Harrison C, Kiladjian JJ, Al-Ali HK, Gisslinger H, Waltzman R, Stalbovskaya V, *et al*. JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. N Engl J Med 2012;366:787-98.
7. James C, Ugo V, Le Couédic JP, Staerk J, Delhommeau F, Lacout C, *et al*. A unique clonal JAK2 mutation leading to constitutive signalling causes polycythaemia vera. Nature 2005;434:1144-8.
8. Baxter EJ, Scott LM, Campbell PJ, East C, Fourouclas N, Swanton S, *et al*. Acquired mutation of the tyrosine kinase JAK2 in human myeloproliferative disorders. Lancet 2005;365:1054-61.
9. Tefferi A, Barbui T. Polycythemia vera and essential thrombocythemia: 2021 update on diagnosis, risk-stratification and management. Am J Hematol 2020;95:1599-613.
10. Scott LM, Tong W, Levine RL, Scott MA, Beer PA, Stratton MR, *et al*. JAK2 exon 12 mutations in polycythemia vera and idiopathic erythrocytosis. N Engl J Med 2007;356:459-68.
11. Pardanani A, Lasho TL, Finke C, Hanson CA, Tefferi A. Prevalence and clinicopathologic correlates of JAK2 exon 12 mutations in JAK2V617F-negative polycythemia vera. Leukemia 2007;21:1960-3.
12. Pikman Y, Lee BH, Mercher T, McDowell E, Ebert BL, Gozo M, *et al*. MPLW515L is a novel somatic activating mutation in myelofibrosis with myeloid metaplasia. PLoS Med 2006;3:e270.
13. Klampfl T, Gisslinger H, Harutyunyan AS, Nivarthi H, Rumi E, Milosevic JD, *et al*. Somatic mutations of calreticulin in myeloproliferative neoplasms. N Engl J Med 2013;369:2379-90.
14. Şahin E, Yönal-Hindilerden İ, Hindilerden F, Aday A, Nalçacı M.

The impact of JAK2V617F mutation on Philadelphia-negative myeloproliferative neoplasms. Turk J Med Sci 2022;52:150-65.
15. Duletić AN, Dekanić A, Hadzisejdić I, Kusen I, Matusan-Ilijas K, Grohovac D, *et al*. JAK2-v617F mutation is associated with clinical and laboratory features of myeloproliferative neoplasms. Coll Antropol 2012;36:859-65.
16. Yönal İ, Dağlar-Aday A, Akadam-Teker B, Yılmaz C, Nalçacı M, Yavuz AS, *et al*. Impact of JAK2V617F mutational status on phenotypic features in essential thrombocythemia and primary myelofibrosis. Turk J Haematol 2016;33:94-101.
17. Borowczyk M, Wojtaszewska M, Lewandowski K, Gil L, Lewandowska M, Lehmann-Kopydłowska A, *et al*. The JAK2 V617F mutational status and allele burden may be related with the risk of venous thromboembolic events in patients with Philadelphia-negative myeloproliferative neoplasms. Thromb Res 2015;135:272-80.
18. Yönal-Hindilerden İ, Şahin E, Hindilerden F, Dağlar-Aday A, Nalçacı M. Clinical impact of JAK2V617F allele burden in Philadelphia-negative myeloproliferative neoplasms. Turk J Haematol 2023;40:174-82.
19. Sassi H, Menif S, Ammar SB, Farrah A, Othmen HB, Amouri H. JAK2 p.(V617F) mutation in Tunisian myeloproliferative neoplasms and its genotype-phenotype correlation. Pan Afr Med J 2021;39:194.
20. Ojeda MJ, Bragós IM, Calvo KL, Williams GM, Carbonell MM, Pratti AF. CALR, JAK2 and MPL mutation status in Argentinean patients with BCR-ABL1- negative myeloproliferative neoplasms. Hematology 2018;23:208-11.
21. Soliman EA, El-Ghlban S, El-Aziz SA, Abdelaleem A, Shamaa S, Abdel-Ghaffar H. JAK2, CALR, and MPL mutations in Egyptian patients with classic Philadelphia-negative myeloproliferative neoplasms. Clin Lymphoma Myeloma Leuk 2020;20:e645-51.
22. AlGhasham N, Alnouri Y, Abalkhail H, Khalil S. Comprehensive analysis of JAK2 mutations: A single center experience. Blood 2014;124:5568.
23. Barbui T, Tefferi A, Vannucchi AM, Passamonti F, Silver RT, Hoffman R, *et al*. Philadelphia chromosome-negative classical myeloproliferative neoplasms: Revised management recommendations from European LeukemiaNet. Leukemia 2018;32:1057-69.
24. Szuber N, Mudireddy M, Nicolosi M, Penna D, Vallapureddy RR, Lasho TL, *et al*. 3023 mayo clinic patients with myeloproliferative neoplasms: Risk-stratified comparison of survival and outcomes data among disease subgroups. Mayo Clin Proc 2019;94:599-610.
25. Randi ML, Ruzzon E, Tezza F, Scapin M, Duner E, Scandellari R, *et al*. JAK2V617F mutation is common in old patients with polycythemia vera and essential thrombocythemia. Aging Clin Exp Res 2011;23:17-21.
26. Vannucchi AM, Antonioli E, Guglielmelli P, Rambaldi A, Barosi G, Marchioli R, *et al*. Clinical profile of homozygous JAK2 617V>F mutation in patients with polycythemia vera or essential thrombocythemia. Blood 2007;110:840-6.
27. Tefferi A, Rumi E, Finazzi G, Gisslinger H, Vannucchi AM, Rodeghiero F, *et al*. Survival and prognosis among 1545 patients with contemporary polycythemia vera: An international study. Leukemia 2013;27:1874-81.
28. Gangat N, Karrar O, Al-Kali A, Begna KH, Elliott MA, Wolanskyj-Spinner AP, *et al*. One thousand patients with essential thrombocythemia: The Mayo Clinic experience. Blood Cancer J 2024;14:11.
29. Loscocco GG, Gesullo F, Capecchi G, Atanasio A, Maccari C, Mannelli F, *et al*. One thousand patients with essential thrombocythemia: The florence-CRIMM experience. Blood Cancer J 2024;14:10.
30. Karantanos T, Chaturvedi S, Braunstein EM, Spivak J, Resar L, Karanika S, *et al*. Sex determines the presentation and outcomes in MPN and is related to sex-specific differences in the mutational burden. Blood Adv 2020;4:2567-76.
31. Godfrey AL, Chen E, Pagano F, Silber Y, Campbell PJ, Green AR. Clonal analyses reveal associations of JAK2V617F homozygosity with hematologic features, age and gender in polycythemia vera and essential thrombocythemia. Haematologica 2013;98:718-21.
32. Du C, Xu Y, Yang K, Chen S, Wang X, Wang S, *et al*. Estrogen promotes megakaryocyte polyploidization via estrogen receptor beta-mediated transcription of GATA1. Leukemia 2017;31:945-56.
33. Landolfi R, Di Gennaro L, Falanga A. Thrombosis in myeloproliferative disorders: Pathogenetic facts and speculation. Leukemia 2008;22:2020-8.
34. Lim Y, Lee JO, Kim SH, Kim JW, Kim YJ, Lee KW, *et al*. Prediction of thrombotic and hemorrhagic events during polycythemia vera or essential thrombocythemia based on leukocyte burden. Thromb Res 2015;135:846-51.
35. Butkiewicz AM, Kemona H, Dymicka-Piekarska V, Matowicka-Karna J, Radziwon P, Lipska A. Platelet count, mean platelet volume and thrombocytopoietic indices in healthy women and men. Thromb Res 2006;118:199-204.
36. Chiusolo P, La Barbera EO, Laurenti L, Piccirillo N, Sorà F, Giordano G, *et al*. Clonal hemopoiesis and risk of thrombosis in young female patients with essential thrombocythemia. Exp Hematol 2001;29:670-6.
37. Tefferi A, Betti S, Barraco D, Mudireddy M, Shah S, Hanson CA, *et al*. Gender and survival in essential thrombocythemia: A two-center study of 1,494 patients. Am J Hematol 2017;92:1193-7.
38. Carobbio A, Thiele J, Passamonti F, Rumi E, Ruggeri M, Rodeghiero F, *et al*. Risk factors for arterial and venous thrombosis in WHO-defined essential thrombocythemia: An international study of 891 patients. Blood 2011;117:5857-9.