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# Insight concerning the MPN driver mutations prevalence in Iraqi myelofibrosis patients

**Mzhr Ali Abbood, Amar Hekmat Mahdi, Yaseen Muhialdeen Taher[1], Al Ani AT Waleed[2]**

**Abstract:**

**BACKGROUND:** The discovery of the Janus kinase 2 (JAK2) in 2005, along with calreticulin (CALR) and myeloproliferative leukemia virus oncogene (MPL) gene mutations, significantly advanced our understanding of primary myelofibrosis (PMF) and other myeloproliferative disorders (MPNs). These mutations are now integral diagnostic markers in the World Health Organization classification of MPNs.

**OBJECTIVES:** The objective of this study was to assess the incidence of JAK2 mutation in Iraqi patients with myelofibrosis (MF).

**MATERIALS AND METHODS:** Eighty patients with MF were enrolled in a cross-sectional study at the National Centre of Hematology, Al-Mustansiriya University, and Hematology Centre in Baghdad Medical City Complex, from February 2024 to November 2024. MPN Molecular Panel mutations were analyzed, with demographic and clinical data collected. Data were presented as frequencies, percentages, means, standard deviations, and ranges. Chi-square ($\chi^2$) test were used for statistical analysis.

**RESULTS:** Eighty patients, 52.5% were male and 47.5% female patients, with a median age of 57.6 years. 66.3% had (PMF), 22.5% had (postpolycythemia vera-MF), and 11.3% had (postessential thrombocythemia-MF). Genetic analysis revealed that 75% had the JAK2V617F mutation, 10% had CALR and MPL mutations, 1.2% had a JAK2 exon 12 mutation, and 3.8% were triple negative.

**CONCLUSIONS:** Mutations in MPN are key molecular markers for diagnosing myelofibrosis (MF), a disease that mainly affects older adults. The JAK2V617F mutation was the most prevalent genetic alteration observed. Fatigue was reported in 93.3% of JAK2, and 100% of CALR- and MPL-mutated patients. Weight loss occurred in 75%, 87.5%, and 50% of JAK2, CALR, and MPL, respectively. Despite arising from distinct genes, these mutations share similar clinical, laboratory, and prognostic outcomes.

**Keywords:**

Iraq, myelofibrosis, myeloproliferative disorder

*Department of Physiology, College of Medicine, Al-Mustansiriya University, [1]The National Center of Hematological Disease Research and Treatment, Al-Mustansiriya University, [2]Department of Community Medicine, College of Medicine, Al-Mustansiriya University, Baghdad, Iraq*

**Address for correspondence:**
Dr. Mzhr Ali Abbood, Department of Physiology, College of Medicine, Al-Mustansiriya University, Baghdad, Iraq.
E-mail: dr_almozhr@yahoo.com

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## Introduction

Primary myelofibrosis (PMF) is a clonal hematopoietic stem cell disorder marked by impaired bone marrow function due to fibrosis. As one of the Philadelphia-negative Myeloproliferative neoplasms (MPNs), PMF shares clinical features with other MPNs, including polycythemia vera (PV) and essential thrombocythemia (ET), although they have distinct clinical histories and treatment strategies. These disorders involve the overproduction of blood cells – red blood cells, white blood cells (WBCs), and platelets.[1]

PMF is a rare condition, occurring with an annual incidence of about 0.3–0.8 per 100,000 persons, which primarily affects adults over 50 years. Approximately 15% of PV and ET patients can transform into a



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PMF-like phenotype, a condition known as post-PV or post-ET MF. Males have a higher incidence, although females tend to have better survival rates. Among MPN disorders, PMF presents the poorest prognosis.[2]

Patients with PMF typically present with severe anemia, hepatosplenomegaly, and constitutional symptoms such as fatigue, fever, and night sweats. They may also experience significant weight loss, bone pain, pruritus, and splenic infarction. PMF patients face an increased risk of hemorrhagic and thrombotic events,[3] along with complications such as ascites, pleural effusion, and portal or pulmonary hypertension.[4] Without treatment, MPN patients face shortened life expectancy due to vascular complications, end-organ damage, bone marrow fibrosis, and progression to acute leukemia.[5]

The discovery of the Janus kinase 2 (JAK2) gene mutation in 2005, along with calreticulin (CALR) and Myeloproliferative Leukemia Virus (MPL) gene mutations, significantly advanced our understanding of PMF and other MPNs, paving the way for targeted therapies.[6] The World Health Organization (WHO) classification of MPNs now includes these mutations as key diagnostic markers.[7]

In 2005, somatic mutation in JAK2 exon 14 (JAK2 V617F) was first reported to occur in over 95% of PV and approximately 50% of ET and PMF patients, resulting in the auto-activation of this tyrosine kinase and enhanced signaling of the downstream JAK-STAT pathway.[8]

The JAK family, which includes JAK1, JAK2, JAK3, and TYK2, is essential for blood cell production, with JAK2 specifically facilitating signaling for hematopoietic growth factors.[9]

The JAK2V617F mutation drives MPN pathogenesis by causing cytokine hypersensitivity and JAK-STAT pathway activation, resulting in erythrocytosis, leukocytosis, thrombocytosis, and splenomegaly.[10] This mutation is common in MPN patients, with more severe manifestations in homozygotes.[11]

The CALR gene on chromosome 19p13.2 encodes a protein that regulates calcium homeostasis and glycoprotein folding.[12] CALR mutations promote cytokine-independent hematopoietic cell growth and activate the JAK-STAT pathway via the MPL receptor, increasing megakaryopoiesis and platelet production.[13,14]

The MPL gene encodes the thrombopoietin receptor (TPOR), crucial for platelet production. Located on chromosome 1p34, it regulates megakaryopoiesis. MPL mutations lead to abnormal cell signaling and contribute to MPN progression.[15]

Patients who are triple negative, meaning they lack JAK2, CALR, and MPL mutations, represent 5%–10% of ET and PMF cases and often have poorer survival outcomes.[7] The study objective was to assess the incidence of MPN driver mutations in Iraqi patients with MF.

## Materials and Methods

A cross-section study was conducted on 80 patients diagnosed with MF study at the National Centre of Hematology, Al-Mustansiriya University, and Hematology and Bone Marrow Transplantation Centre in Baghdad Medical City Complex, starts from February 2024 to November 2024.

Patients previously diagnosed with MF according to the WHO criteria were included. Patient information was collected based on presenting complaints, clinical characteristics, complete blood count (CBC), genetic workup, bone marrow study, and ultrasound for splenomegaly and hepatomegaly were all studied.

All features and studies included were based on medical records at the time of diagnosis.Additionally, CBC results, genetic workup, and ultrasound findings for splenomegaly and hepatomegaly were analyzed from both the initial diagnosis and during the course of the study. This study assessed the presence of JAK2V617F, CALR, MPL, and EXON 12 mutations in MF patients over the period from February to November 2024.

DNA was extracted using either the QIAamp DNA Micro Kit (QIAGEN, Germany) or ReliaPrep Blood gDNA Miniprep system (Promega, USA), with 200 µL of blood yielding 100 µL of DNA. DNA quantity and purity were assessed using a Qubit spectrophotometer.

Additionally, MPN driver mutations were analyzed using the SNP biotechnology MPN screening kit (Turkey),

**Table 1: The oligonucleotide sequence used for the identification of JAK2V617F mutations**

| Primer | Direction | Length (bp) | Sequence |
|---|---|---|---|
| V617F-Forward | Forward | 21 | 5'-TCCTCAGAACGTTGATGGCAG-3' |
| V617F-Fwt | Forward | 28 | 5'-GCATTTGTTTTAAATTATGGAGTATATG-3' |
| V617F-Reverse | Reverse | 23 | 5'-ATTGCTTTCCTTTTTCACAAGAT-3' |
| V617FRmt | Reverse | 27 | 5'-GTTTTACTTACTCTCGTCTCCACAAAA-3' |

FWT=Forward wild type, Rmt=Reverse mutant (Schnittger *et al*.,)[15]

which detects mutations with high sensitivity (below 1% mutant allele detection). JAK2V617F mutation was analyzed using quantitative real-time PCR, with the reaction monitored through FAM dye for mutation detection and HEX dye as an internal control [Table 1].

Allele-specific PCR was also conducted using four primers to amplify three PCR products, and PCR results were resolved on 2% agarose gel. Real-time PCR utilized FAM, HEX, Texas Red, and CY5 fluorescence dyes for mutation detection.

Eighty patients with MF were enrolled in a cross-sectional study conducted at the National Centre of Hematology, Al-Mustansiriya University, and the Hematology Centre at Baghdad Medical City Complex from March to November 2024.

Official approval to conduct this research was obtained from the relevant authority, as per letter no. 21/995 dated March 3, 2024, issued by Al-Mustansiriya University, following the review and ethical clearance of the research proposal, and adhered to the guidelines set by the Iraqi Ministry of Health.

All participants gave their permission to take part in the study after everything was clearly explained to them, including the purpose, steps, possible risks, and benefits. They were told their information would stay private, and all individuals were informed of their right to withdraw from the study at any time without any consequences.

### Statistical analysis

The collected data were coded, entered, presented, and analyzed using the IBM SPSS-29 statistical software (IBM Corporation, Armonk city, New York, USA). Data were presented as frequencies, percentages, means, and standard deviations. Statistical significance was assessed using the Student's *t*-test, paired *t*-test, or analysis of variance for quantitative data, and the Pearson Chi-square or Fisher's exact test for qualitative data.

## Results

### General characteristics

A total of 80 patients were diagnosed with MF, of which 52.5% were male and 47.5% female. The mean age of the participants was 57.6 years, with an age range of 26–79 years. The highest number of patients were in the 50–59-year age group, while the least number of patients were in the under-40 age group [Table 2].

**Table 2: Demographic characteristic of patients enrolled in the study**

| Characteristic | *n* (%) |
|---|---|
| Age (years) | |
| <40 | 5 (6.3) |
| 40 | 8 (10.0) |
| 50 | 30 (37.5) |
| 60 | 24 (30.0) |
| ≥70 | 13 (16.3) |
| Mean±SD (range) | 57.6±11.0 (26–79) |
| Gender | |
| Male | 42 (52.5) |
| Female | 38 (47.5) |
| Diagnosis | |
| PMF | 53 (66.3) |
| TPV | 18 (22.5) |
| TET | 9 (11.3) |

SD=Standard deviation, PMF=Primary myelofibrosis, PPV-MF =Transformed polycythemia Vera myelofibrosis, PET-MF = post-polycythemia vera myelofibrosis

The diagnoses included 53 patients (66.3%) with PMF, 18 patients (22.5%) with myelofibrotic transformation postpolycythemia vera-MF (PPV-MF), and 9 patients (11.3%) with postessential thrombocythemia-MF (PET-MF).

### Myeloproliferative disorder driver mutation incidence in Iraqi myelofibrosis patients

The study revealed the genetic mutation profile of the MF patients in line with the WHO diagnostic criteria.

**Table 3: Comparison of the characteristics of patients with JAK2V617F, calreticulin, and myeloproliferative leukemia virus oncogene mutations**

| Characteristic | JAK2V617F (*n*=60), *n* (%) | CALR (*n*=8), *n* (%) | MPL (*n*=8), *n* (%) | *P* |
|---|---|---|---|---|
| Age (years) | | | | |
| <40 | 3 (5.0) | 1 (12.5) | 1 (12.5) | 0.800 |
| 40–49 | 6 (10.0) | - | 1 (12.5) | |
| 50–59 | 24 (40.0) | 2 (25.0) | 3 (37.5) | |
| 60–69 | 16 (26.7) | 3 (37.5) | 3 (37.5) | |
| ≥70 | 11 (18.3) | 2 (25.0) | - | |
| Mean±SD (range) | 57.7±10.7 (26–76) | 61.0±13.8 (35–79) | 53.8±12.2 (28–66) | 0.432 |
| Gender | | | | |
| Male | 29 (48.3) | 3 (37.5) | 7 (87.5) | 0.081 |
| Female | 31 (51.7) | 5 (62.5) | 1 (12.5) | |

The Chi-square test, Student's *t*-test, and ANOVA were all utilized in the study as appropriate for the data analysis. SD=Standard deviation, CALR=Calreticulin, MPL=Myeloproliferative leukemia virus oncogene

Among the participants, 75% (60 patients) tested positive for the JAK2V617F mutation, 10% (8 patients) for CALR mutations, and 10% (8 patients) for MPL mutations.

A small proportion of patients exhibited JAK2 exon 12 mutations (1.2%), and 3.8% were triple negative. This analysis of mutation types aims to further investigate how these genetic profiles may influence clinical outcomes. Demographically, the study found no significant age differences among patients with JAK2V617F, CALR, or MPL mutations. In contrast, gender distribution varied significantly between these mutation groups [Table 3].

A higher proportion of females (62.5%) carried the CALR mutation, while a larger percentage of males (87.5%) had MPL mutations. No gender preference was observed in the JAK2V617F group.

**Table 4: Comparison of clinical features in Janus kinase 2, calreticulin, and myeloproliferative leukemia virus oncogene mutated myelofibrosis**

| Clinical feature | JAK2 (*n*=60), *n* (%) | CALR (*n*=8), *n* (%) | MPL (*n*=8), *n* (%) | *P* |
|---|---|---|---|---|
| Fatigue | | | | |
| Yes | 56 (93.3) | 8 (100) | 8 (100) | 0.570 |
| No | 4 (6.7) | - | - | |
| Weight loss | | | | |
| Yes | 45 (75.0) | 7 (87.5) | 4 (50.0) | 0.206 |
| No | 15 (25.0) | 1 (12.5) | 4 (50.0) | |
| Night sweat | | | | |
| Yes | 38 (63.3) | 7 (87.5) | 5 (62.5) | 0.392 |
| No | 22 (36.7) | 1 (12.5) | 3 (37.5) | |
| Abdominal pain | | | | |
| Yes | 28 (46.7) | 2 (25.0) | 5 (62.5) | 0.315 |
| No | 32 (53.3) | 6 (75.0) | 3 (37.5) | |
| Bleeding tendency | | | | |
| Yes | 9 (15.0) | - | 1 (12.5) | 0.498 |
| No | 51 (85.0) | 8 (100) | 7 (87.5) | |
| Other presentations | | | | |
| Yes | 14 (23.3) | 3 (37.5) | 3 (37.5) | 0.089 |
| No | 46 (76.7) | 5 (62.5) | 5 (62.5) | |

CALR=Calreticulin, MPL= Myeloproliferative Leukemia Virus (MPL) gene, JAK 2 = Janus kinase 2

Patients commonly presented with clinical symptoms such as fatigue, unexplained weight loss, night sweats, abdominal pain, and an increased tendency to bleed. Fatigue was the most prevalent symptom, observed in 93.3% of JAK2-mutated patients, 100% of CALR-mutated patients, and 100% of MPL-mutated patients [Table 4].

Weight loss was present in 75% of JAK2-mutated patients, 87.5% of CALR-mutated patients, and 50% of MPL-mutated patients. Night sweats were reported by 63.3% of JAK2-mutated, 87.5% of CALR-mutated, and 62.5% of MPL-mutated patients.

Laboratory data for the study population revealed no significant differences in WBC count, hemoglobin (Hb), or platelet levels among the mutation groups, both at diagnosis and at the time of evaluation [Table 5].

However, JAK2V617F-positive patients showed significantly lower Hb levels ($P = 0.001$) compared to CALR ($P = 0.923$) and MPL ($P = 0.642$) mutation carriers.

Additionally, platelet counts were significantly higher in JAK2V617F-positive patients ($P = 0.0001$), with no similar trends in the CALR and MPL groups. No significant changes were found in total leukocyte count or WBC counts between the different mutation groups.

The comparison of initial and recent laboratory values indicated a significant difference in Hb levels in JAK2-mutated patients ($P = 0.001$), but not in CALR or MPL groups.

Platelet counts were also significantly higher at diagnosis compared to the time of the study in JAK2 and CALR mutation patients.

Among the 58 patients with the JAK2V617F mutation, 36 (60%) were diagnosed with PMF, 17 (28.3%) with PPV-MF, and 7 (11.7%) with PET-MF. Of the 8 patients with CALR mutations, 7 (87%) were diagnosed with PMF and 1 (12.5%) with PET-MF.

**Table 5: Comparison of the laboratory characteristics of Janus kinase 2, calreticulin, and myeloproliferative leukemia virus oncogene**

| Laboratory investigation | JAK2 (*n*=60) | CALR (*n*=8) | MPL (*n*=8) | *P* |
|---|---|---|---|---|
| WBC (×10³ cells/μL), mean±SD | | | | |
| At diagnosis | 8.59 (2.0–35.5) | 9.85±6.07 (3.2–21.0) | 12.53±9.37 (3.0–33.5) | 0.465 |
| Last | 11.84±7.99 (2.1–33.0) | 7.85±5.77 (4.3–21.0) | 9.08±9.80 (2.0–32.3) | 0.315 |
| Hb (g/L) | | | | |
| At diagnosis | 9.71±1.99 (6.3–12.2) | 10.63±2.97 (7.3–17.1) | 10.63±2.97 (7.3–17.1) | 0.409 |
| Last | 9.98±2.03 (5.7–14.3) | 9.79±1.74 (8.0–12.7) | 11.03±2.75 (7.7–16.0) | 0.384 |
| Platelets (×10³ platelets/μL) | | | | |
| At diagnosis | 437.15±280.69 (90–1128) | 469.63±337.00 (82–978) | 451.38±375.13 (122–1097) | 0.954 |
| Last | 253.33±197.26 (30–1091) | 182.25±163.58 (33–463) | 309.00±236.26 (86–759) | 0.442 |

The Chi-square test and Student's *t*-test were both utilized as appropriate for the data analysis. CALR=Calreticulin, MPL=Myeloproliferative leukemia virus oncogene, JAK 2=Janus kinase 2, SD=Standard deviation, Hb=Hemoglobin, WBC=White blood cell

**Table 6: Frequency of different mutations with primary or postpolycythemia vera or postessential thrombocythemia-myelofibrosis**

| Diagnosis | JAK2 (*n*=60), *n* (%) | CALR (*n*=8), *n* (%) | MPL (*n*=8), *n* (%) | *P* |
|---|---|---|---|---|
| PMF | 36 (60.0) | 7 (87.5) | 7 (87.5) | 0.261 |
| Post-PV-MF | 17 (94.4) | - | - | |
| Post-ET-MF | 7 (11.7) | 1 (12.5) | 1 (12.5) | |

CALR=Calreticulin, MPL=Myeloproliferative leukemia virus oncogene, JAK 2=Janus kinase 2, PMF=Primary myelofibrosis, MF=Myelofibrosis, PV=Polycythemia vera, ET=Essential thrombocythemia

Similarly, 7 (87.5%) of the 8 MPL-mutated patients had PMF, with 1 (12.5%) diagnosed with PET-MF.

There were no significant differences observed in mutation distribution among PPV-MF and PET-MF patients across JAK2, CALR, and MPL mutations [Table 6].

## Discussion

The identification of somatic driver mutations in JAK2 (V617F and exon 12), CALR, and MPL (W515 L/K) has significantly the diagnostic framework for myeloproliferative neoplasms (MPNs), as underscored in the WHO classification.[7]

In this study, 53 patients (66.3%) were diagnosed with PMF, and 36.3% with 33.7% transformation MF, 18 patients (22.5%) with myelofibrotic transformation from PPV-MF, and 9 patients (11.2%) with PET-MF. These findings are consistent with those reported by Luque Paz *et al*., who identified 63.7% of cases as PMF and 36.3% as transformation PPV-MF and PET-MF.[16]

JAK2 V617F, the first mutation definitively linked to MPN pathogenesis, was the most common mutation, observed in 60 patients (75%). In agreement with the present findings, previous studies conducted by Basim Maysam *et al*. in Kurdistan,[17] Lavi,[18] and Rozovski *et al*.[19] reported comparable results. Specifically, these studies observed that approximately 60% of patients with PMF in their respective cohorts harbored the JAK2V617F gene mutation.[17-19] Study findings are consistent with those reported in the existing literature.

Mutations in the CALR gene were first identified in 2013 in patients with ET and MF. Over 36 distinct frameshift mutations in exon 9, caused by insertions or deletions, have been documented.[20] CALR mutations are mutually exclusive with JAK2 and MPL mutations in MF patients. In the present cohort, CALR mutations were detected in approximately 10% of MF patients. Montero in 2022 reported a frequency of 15.4% in PMF patients.[21] The value observed was slightly higher than in the current study, potentially due to the increased frequency of JAK2V617F mutations in PMF patients from Iraq.

MPL encodes the TPOR, a key protein involved in platelet production. The MPL gene is located on chromosome 1, specifically in exon 10, and encodes a protein consisting of 635 amino acids. Mutations in the MPL gene have been reported in approximately 5%–10% of patients with PMF.[22] In the present study, MPL mutations were observed in 10% of patients with MF and in 13.2% of patients with PMF. Beer *et al*. investigated the frequency of MPL mutations in PMF patients and reported that approximately 7% of patients in their cohort harbored MPL mutations.[23] Guglielmelli *et al*.'s study reported a frequency of 8.2% for MPL mutations in patients with PMF.[24]

The higher MPL mutation frequency in the current study cohort may be explained by methodological differences. Unlike Philip *et al*., who applied a *P* value threshold of < 0.01 and limited their analysis to anemic MF patients, the current study included both anemic and non-anemic cases, potentially capturing a broader mutation spectrum.

Approximately 10%–15% of PMF patients lack any of the three primary mutations (JAK2, CALR, and MPL) and are classified as "triple negative." Study, identified triple-negative cases in 3 patients (3.8%), which is lower than the prevalence reported by Jang MA & Choi CW. [25] This difference may be attributed to the fact that the study by Jang MA *et al*. focused solely on PMF, whereas the current study included both PMF and transformed MF subtypes.

In this study, the constitutional symptoms were present in all patients (100%) at the time of diagnosis, with varying frequencies for each symptom. Fatigue (95%), weight loss (73.8%), night sweats (63.7%), abdominal discomfort (46.3%), bleeding tendency (12.5%), and other nonspecific symptoms (27.5%) were most commonly reported. Pakistani researchers reported a similar result as they found that 90% of the patients in their group were symptomatic at the diagnosis, and they presented with constitutional symptoms.[26]

Literature had shown that splenomegaly is mainly associated with the JAK2 mutation, and the presence of JAK2 mutation is essential for the spleen size to increase.[27] Meanwhile, another study had shown that 8.1% of the JAK2-mutated PMF patients and 25% of MPL-mutated patients have had splenomegaly at diagnosis. Splenomegaly was not observed in patients with CALR mutations.[18]

Notably, in this study, the genetic analysis revealed a higher prevalence of constitutional symptoms in JAK2-mutated patients compared to those with CALR and MPL mutations and showed no difference in the

clinical presentation of patients carrying JAK2, CALR, or MPL mutations. However, night sweats and abdominal discomfort due to increased spleen span were more frequently observed in CALR-mutated patients.

This study confirmed that most JAK2-mutated patients and all CALR- and MPL-mutated PMF patients had splenomegaly at the diagnosis. The current study data were higher than what was reported by others. This result is explained by the stronger inflammatory response and more aggressive disease course associated with JAK2 mutations. In CALR, mutations may lead to altered immune responses and cytokine production in certain populations, contributing to symptoms like night sweats even without the classic splenomegaly seen in JAK2-mutated patients.

Furthermore, during patient history assessment, individuals with JAK2 mutations exhibited a lower frequency of bleeding tendencies compared to those with MPL and CALR mutations. On the other hand, patients harboring CALR mutations were at an increased risk of developing ischemic heart disease and heart failure compared to those with JAK2 or MPL mutations. Conversely, a meta-analysis on PMF by published in 2016 indicated that patients with CALR mutations have a lower risk of thrombosis and a reduced incidence of cardiovascular diseases, including heart failure,[28] which differ from those of the present study.

The observed differences may be attributed to variations in study design and sample size. The study by Pei *et al*.[28] was a meta-analysis involving a large size cohort, whereas the current study is a cross-sectional analysis with a smaller sample size. Additionally, the differences compared to the findings of Maysam *et al*.,[17] conducted in Kurdistan, may be due to differing inclusion criteria: their study focused solely on PMF within Ph-negative MPNs, while the present study includes both PMF and transformed MF subtypes.

Numerous studies have investigated the impact of JAK2, CALR, and MPL mutations on various hematological parameters in MF patients. The cytopenic phenotype predominates over the myeloproliferative phenotype and is more commonly associated with PMF, whereas the myeloproliferative phenotype is typically observed in secondary MF, PET-MF, and PPV-MF.[29] Researchers have reported that patients with CALR mutations exhibit a lower risk of developing anemia, thrombocytopenia, and marked leukocytosis compared to those with JAK2 and MPL mutations.[30]

Conversely, this study observed no significant differences in the levels of Hb, leukocytes, and platelets among the three types of driver mutations examined in this study. These findings are consistent with those of Basim Najm *et al*.,[17] conducted in Kurdistan, which also reported no differences in hematological parameters between PMF patients harboring JAK2, CALR, or MPL mutations.

## Conclusions

Mutations study in MPN are important molecular markers for the diagnosis of MF, JAK2, CALR, and MPL genes serve as critical molecular markers in the diagnosis of MF. JAK2V617F was found in 75%, CALR and MPL in 10% each, JAK2 exon 12 in 1.2%, and 3.8% were triple-negative.

Fatigue was the most prevalent symptom, observed in 93.3% of JAK2-mutated patients, 100% of CALR-mutated patients, and 100% of MPL-mutated patients. Weight loss was present in 75% of JAK2-mutated patients, 87.5% of CALR-mutated patients, and 50% of MPL-mutated patients. There were no significant differences observed in mutation distribution among PPV-MF and PET-MF patients across JAK2, CALR, and MPL mutations.

Regarding the distribution of JAK2, CALR, and MPL mutations between PPV-MF and PET-MF cases, no significant differences in phenotype features were observed.

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### Conflicts of interest
There are no conflicts of interest.

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