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Journal of Bioscience and Applied Research
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Hematological parameters in Myeloproliferative neoplasms in Sudanese patients

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DOI:10.21608/jbaar.2024.380714

Abstract

The new International Consensus Classification (ICC) for Myeloid Neoplasms and Acute Leukemias was updated in 2022 by the World Health Organization (WHO). This includes the following conditions: essential thrombocythemia (ET), polycythemia vera (PV); primary myelofibrosis, MPN, unclassifiable (MPN-U); chronic myeloid leukemia (CML); chronic neutrophilic leukemia (CNL); and chronic eosinophilic leukemia. Nonetheless, there are three core subtypes of classical myeloproliferative neoplasms (MPN): essential thrombocythemia (ET), polycythemia vera (PV), and primary myelofibrosis (1). Effective treatment for this illness is frequently delayed by incorrect diagnoses. The current study assessed the contribution of routine blood tests to the precise diagnosis of MPN. Blood analysis was done on 101 adult MPN Sudanese patients in total. Eight standard blood parameters were analyzed using a Sysmex XE-2100TM machine. The values were compared across the subcategories, and a difference that was deemed statistically significant was defined as a value of $P<0.05$. The patients' median hemoglobin, platelet, and red blood cell counts were 523x103, 15.4 g/dl, and 5.7x109/l, respectively. There were noticeable variations between the subcategories. The current study demonstrated that the key component of accurately diagnosing MPNs according to WHO classifications is the evaluation of peripheral blood cells' blood routine parameters.

Keywords: Myeloproliferative neoplasms, blood routine examination, diagnosis.

Introduction:

Primary myelofibrosis (PMF), essential thrombocythemia (ET), polycythemia vera (PV), and chronic myelogenous leukemia are among the clonal hematological malignancies referred to as myeloproliferative neoplasms (MPNs)(1,2). The World Health Organization (WHO) guidelines state that MPN is the authorized terminology (3). The clonal proliferation of aberrant hematopoietic stem cells is a characteristic of MPNs (4). The terms "Philadelphia-negative classical MPNs" refer to PV, ET, and PMF as a collective group of these three disease types.

The prevalence of PV (44–57 per 100,000), which was higher in men than in women (male–to–female 1.8:1), and ET (38–57 per 100,000) was significantly higher than that of MF (4-6 per 100,000) or subgroups comprising MF (post–PV MF = 0.3–0.7 per 100,000; post–ET MF = 0.5–1.1 per 100,000) (5). Men and women both have almost the same overall incidence of myelofibrosis (MF). Men are slightly more often than women to have PV (male-

Received: June 26, 2024. Accepted: September 9, 2024. Published: September 20, 2024

to-female ratio: 1.8:1), but women are more likely than men to have ET (male-to-female ratio: 1:2). Although MPNs may occur to anyone at any age, the majority of patients diagnosed with MPN after the age of 60. The median age at which PMF, ET, and PV diagnoses are made is 65 years old, 56 years old, and 61 years old, respectively.

The 2008 WHO criteria, which were amended, use a mix of clinical, morphological, and molecular evaluation to diagnose MPN. Increased red blood cell (RBC) production in PV, prolonged thrombocytosis in ET, and bone marrow (BM) fibrosis in PMF are the hallmarks of Philadelphia chromosome-negative MPN (6). Occurring MPN patients can occasionally have normal blood counts due to splenomegaly, gastrointestinal bleeding, and iron shortage, or early stage of the disease (7). Careful evaluation is required in cases of clinically questionable MPN, such as intra-abdominal thrombosis with normal blood counts (8). This study aims to analyze the hematological features of Sudanese patients diagnosed with MPN at the Radiation and Isotopes Centre Khartoum (RICK) from 2016 to 2019.

MATERIALS AND METHODS

This was a cross-sectional descriptive hospital-based study**,** conducted at the Radiation and Isotopes Centre Khartoum (RICK), Khartoum, Sudan, from May 2016 to September 2017. The study was approved by the ethics committee of the Ministry of Health's research department and Alneelin University. Informed written consent was obtained from all the patients before collection of samples.

A total of 101 patients with chronic MPNs were enrolled in this study. The patients were diagnosed based on 2008 World Health Organization (WHO) criteria (1), 63.4% were diagnosed with PV, 23.8% with ET, and 12.8%. with MF.

Five milliliters of peripheral blood were collected from each subject in K3 EDTA vacutainer tubes. Samples were processed immediately after collection. The complete blood counts (CBC) were performed using an Automated Hematology Analyzer (Sysmex 21). The CBC included measurements of hemoglobin, hematocrit, total white blood cell count, platelet counts, red blood cell counts, mean cell volume, mean cell hemoglobin, and mean cell hemoglobin concentration.

The statistical analysis of the results was done using SPSS (version 23) software. A one-way ANOVA test was used to compare the variation between the groups and within them. A p-value of less than 0.05 was considered statistically significant.

RESULTS

101 MPN patients had the following baseline characteristics: 48 (47.5%) and 53 (52.5%) were female. The median age of all Sudanese patients was 52 years old (range: 25-85 years old). Of the total, 63.4% had PV, 23.8% had ET, and 12.8% had MF as their diagnosis. There were differences in hemoglobin, leukocyte, and platelet counts among the various illness subgroups. The study population's hematological characteristics are shown in (Table 1). Patients with MPN had significantly greater platelet counts, RBC counts, and hemoglobin levels ($p<0.0001$). Though this difference was not statistically significant ($p=0.772$), platelets were lower in MF patients. The WBC count was either normal or slightly elevated; for ET ($p=0.229$) and MF ($p=0.398$), this result was not statistically significant. On the other hand, PV patients' WBC count was statistically significant ($p=0.05$).

Table 1 Comparison of Laboratory Characteristics in Patients with PV, ET, MF.

Variable	PV (n=64)		ET (n=24)		MF (n=13)	
	median (range)	P value	median (range)	P value	median (range)	P value
Platelets count X 10^9/L	368 (170-1901)	0.0001	969 (362-1800)	0.0001	452.5 (139-1283)	0.772
WBCs count X 10^9/L	7.8 (4.4-18.4)	0.05	9.8 (3.8-23)	0.229	8.1 (2.6-63)	0.398
RBCs count X 10^{12}/L	6.0 (4.9-9.4)	0.0001	4.9 (3.4-8.4)	0.106	4.7 (2.8-6.7)	0.0004
Hb (g/dl	16 (13.6-20)	0.0001	12.9 (8-17.3)	0.004	12.8 (7.9-15)	0.0004
Hct (%)	50 (42.2-60.4)	0.0001	43 (29-58)	0.014	40.5 (26-48)	0.0003
MCV (fl)	84 (70-95)	0.445	81 (68-97)	0.401	89 (79-91)	0.023
MCH (pg)	27 (21-31)	0.0899	25 (19-29)	0.068	27 (24-32)	0.903
MCHC (g/dl)	31 (29-36)	0.0001	30 (25-33)	0.024	30 (21-31)	0.010

* P<0.05 indicates a statistically significant difference. MPN (myeloproliferative neoplasms), Polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF).

DISCUSSION

A distinct subset of hematological malignancies is myeloproliferative neoplasms or MPNs. Since the diagnosis of this disease might frequently lack precise diagnostic markers, particularly in the early stage, the first line of diagnosis depends on the clinical lab results in addition to molecular and genetic investigation (8). The goal of this study is to demonstrate how important routine blood cell analysis is for correctly diagnosing myeloproliferative diseases.

The study group was divided into three groups: 63.4% of the patients were diagnosed with pulmonary vein disease, 23.8% had erectile dysfunction, and 12.8% had myocardial fibrillation. The presented results are marginally lower than the findings published by Mishcheniuk OY et al, who assessed the blood parameters in a sample of 85 patients diagnosed with polycythemia vera (PV), 43 patients diagnosed with essential thrombocythemia (ET), and 40 patients diagnosed with primary myelofibrosis (PMF)(9). Hematological features of the 101 specimens, the findings of this investigation disclosed both commonalities and significant disparities in comparison to studies carried out at both national and worldwide levels. For example, research undertaken in Sudan According to two investigations by Sahar et al. examining the clinical characteristics of Philadelphia-negative myeloproliferative neoplasms in Sudan,

polycythemia vera (PV) was shown to be the most prevalent subtype, with patients' mean age in the early 50s (10). Comparing the current study results to that of Enbolm et al., who reported a slightly larger proportion of males in the PV and MF groups and a predominance of females in the ET cohort, the latter study likewise found a broadly balanced gender distribution. In terms of the disease subtype distribution, the current study's (63.4%) larger proportion of PV was reported in comparison to the Ejim study's (44.4% ET, 40.7% PV, and 14.9% MF) findings(11).

Based on the current investigation, various disease subtypes had variable levels of hemoglobin, leukocytes, red blood cells, and platelets. The platelet count, red blood cell count, and hemoglobin levels were reported to be considerably higher in patients with MPN ($p < 0.0001$). This finding aligns with the findings of Mishcheniuk OY et al. and Mattar MM et al. (9, 12), In their investigation of 222 patients, Zohu et al. found a statistically significant positive link between MPNs and rising hemoglobin levels, but no significant correlation with platelet count(13). Furthermore, Zahang et al. observed a statistically significant positive link between their particular study group of PV patients and higher hemoglobin percentage levels (14). Patients diagnosed with essential thrombocythemia (ET) generally have reduced total white blood cell (leukocyte) counts and increased levels of hemoglobin(15).

A prior investigation revealed that CALR mutations were linked to a younger age, increased platelet count, reduced risk of thrombosis, decreased leukocytosis, and a lower likelihood of requiring transfusion treatments(16). The results of our study on individuals with CALR mutations indicated a propensity for increased platelet levels and reduced need for transfusions. However, these statistically insignificant differences are probably attributable to the limited size of the sample. Nevertheless, our investigation did not reveal any clear inclination toward younger age in individuals with PMF who had CALR mutations. Among individuals with ET, mutations in the CALR gene have been associated with reduced leukocytosis, decreased hemoglobin levels, and increased platelet counts. Previous studies have consistently shown that individuals diagnosed with myelofibrosis (PMF) who had CALR mutations have elevated platelet levels and improved survival rates (17, 18). Furthermore, individuals diagnosed with essential thrombocythemia (ET) who had CALR mutations have been linked to increased platelet counts but decreased hemoglobin levels (19, 20). The objective of this work is to highlight the diagnostic significance of regular blood parameter analysis in categorizing MPN subtypes based on WHO-specific criteria. The findings of the study were consistent with several previously published investigations. Nevertheless, the variations in the findings in comparison to other studies can be attributed to distinct illness patterns, heterogeneous demographics, and genetic factors. Subsequent investigations require a more extensive sample size to authenticate the scientific findings.

Conflict of Interest:

All authors declare that they have no conflict of interest.

Funding: **None**

REFERENCES:

1. Thiele J, Kvasnicka HM, Orazi A, Gianelli U, Gangat N, Vannucchi AM, et al. The international consensus classification of myeloid neoplasms and acute Leukemias: myeloproliferative neoplasms. Am J Hematol. 2023;98(1):166-79.
2. Abu Rakhey, M., Abd El-Kareem, S., Ma, D. Folic Acid Conjugated Graphene Oxide Graviola Nanoparticle for Sono-Photodynamic Leukemia Treatment: Up-To-Date Cancer Treatment Modality. *Journal of Bioscience and Applied Research*, 2022; 8(1): 28-45. doi: 10.21608/jbaar.2022.223360

3. 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(20):2391-405.
4. Choi CW, Bang SM, Jang S, Jung CW, Kim HJ, Kim HY, et al. Guidelines for the management of myeloproliferative neoplasms. Korean J Intern Med. 2015;30(6):771-88.
5. Mehta J, Wang H, Iqbal SU, Mesa R. Epidemiology of myeloproliferative neoplasms in the United States. Leuk Lymphoma. 2014;55(3):595-600.
6. Campo E, Swerdlow SH, Harris NL, Pileri S, Stein H, Jaffe ES. The 2008 WHO classification of lymphoid neoplasms and beyond: evolving concepts and practical applications. Blood. 2011;117(19):5019-32.
7. Austin SK, Lambert JR. The JAK2 V617F mutation and thrombosis. Br J Haematol. 2008;143(3):307-20.
8. Sarid N, Eshel R, Rahamim E, Carmiel M, Kirgner I, Shpringer M, et al. JAK2 mutation: an aid in the diagnosis of occult myeloproliferative neoplasms in patients with major intraabdominal vein thrombosis and normal blood counts. Isr Med Assoc J. 2013;15(11):698-700.
9. Mishcheniuk OY, Klymenko SV. Predictive value of laboratory hematological parameters for thromboses development in patients with spontaneous and radiation associated Ph negative myeloproliferative neoplasms. Probl Radiac Med Radiobiol. 2015;20:376-98.
10. Elbager S, Abdelgader E, Ali S, Mursal T, Yousif N, Osman E, et al. Clinical Manifestations of Philadelphia-negative Myeloproliferative Neoplasms in Sudan. Journal of Bioscience and Applied Research. 2018;4:98-105.
11. Enblom A, Lindskog E, Hasselbalch H, Hersby D, Bak M, Tetu J, et al. High rate of abnormal blood values and vascular complications before diagnosis of myeloproliferative neoplasms. Eur J Intern Med. 2015;26(5):344-7.
12. Mattar MM, Morad MA, El Husseiny NM, Ali NH, El Demerdash DM. Correlation between JAK2 allele burden and pulmonary arterial hypertension and hematological parameters in Philadelphia negative JAK2 positive myeloproliferative neoplasms. An Egyptian experience. Ann Hematol. 2016;95(10):1611-6.
13. Zhou S, Tremblay D, Hoffman R, Kremyanskaya M, Najfeld V, Li L, et al. Clinical Benefit Derived from Decitabine Therapy for Advanced Phases of Myeloproliferative Neoplasms. Acta Haematol. 2021;144(1):48-57.
14. Zhang Y, Zhou Y, Wang Y, Teng G, Li D, Wang Y, et al. Thrombosis among 1537 patients with JAK2(V617F) -mutated myeloproliferative neoplasms: Risk factors and development of a predictive model. Cancer Med. 2020;9(6):2096-105.
15. Rumi E, Boveri E, Bellini M, Pietra D, Ferretti VV, Sant'Antonio E, et al. Clinical course and outcome of essential thrombocythemia and prefibrotic myelofibrosis according to the revised WHO 2016 diagnostic criteria. Oncotarget. 2017;8(60):101735-44.
16. Tefferi A, Gangat N, Pardanani A, Crispino JD. Myelofibrosis: Genetic Characteristics and the Emerging Therapeutic Landscape. Cancer Res. 2022;82(5):749-63.
17. Tefferi A, Lasho TL, Finke CM, Knudson RA, Ketterling R, Hanson CH, et al. CALR vs JAK2 vs MPL-mutated or triple-negative myelofibrosis: clinical, cytogenetic and molecular comparisons. Leukemia. 2014;28(7):1472-7.
18. 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(25):2379-90.

19. Narlı Özdemir Z, İpek Y, Patır P, Ermiş G, Çiftçiler R, Özmen D, et al. Impact of CALR and JAK2V617F Mutations on Clinical Course and Disease Outcomes in Essential Thrombocythemia: A Multicenter Retrospective Study in Turkish Patients. Turk J Haematol. 2024;41(1):26-36.
20. Nangalia J, Massie CE, Baxter EJ, Nice FL, Gundem G, Wedge DC, et al. Somatic CALR mutations in myeloproliferative neoplasms with nonmutated JAK2. N Engl J Med. 2013;369(25):2391-405.