Frequency and Clinicohaematological Pattern of Myeloproliferative Neoplasms Among Patients Presenting in Tertiary Care Hospital

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Abstract

Objective: To determine the frequency and Clinico-haemtological pattern of myeloproliferative neoplasms (MPNs) among patients presenting in a Tertiary Care Hospital of Lahore

Material and Methods: This cross sectional study was conducted on 241 patients presenting in Hematology Department of Jinnah Hospital Lahore ***r*** for bone marrow biopsy after taking approval from IRB. Frequency of myeloproliferative diseases like Chronic myelogenous leukemia, Polycythemia Vera, Essential thrombocythemia, Primary Myelofibrosis was determined and main clinical and hematologic patterns among patients of myeloproliferative neoplasms were noted. Data analysis was done using SPSS. Qualitative variables were presented as frequency and percentages, quantitative variables were presented as mean and SD. Data was stratified for age and gender, post stratification chi square was applied and p </= 0.05 was taken as significant.

Results: In this study, frequency of MPNs in patients presenting for bone marrow biopsy was found to be 31.54%. Frequency of different MPNs in the 241 patients presenting for bone marrow biopsy were as follows; Chronic myelogenous leukemia was found in 53, Polycythemia Vera in 13, Essential thrombocythemia in 06 and Primary Myelofibrosis in 04 patients. Frequency of various clinico-hematological patterns shows pallor 82.89%, followed by weight loss 80.26%, fever 73.68%, hepatomegaly 32.89%, splenomegaly 19.18%. bleeding 15.79%, and visual disturbance 14.47%. Among hematological parameters anemia was present in 69.74% followed by leukocytosis 31.51%, and thrombocytopenia in 21.05%

Conclusion: This study concluded that frequency of myeloproliferative neoplasms in patients presenting for bone marrow biopsy was 31.54% with chronic myelogenous leukemia being the most common followed by polycythemia vera, essential thrombocythemia and primary myelofibrosis.

Keywords: Myeloproliferative Neoplasms, Chronic Myelogenous Leukemia, Primary Myelofibrosis.

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Introduction

A class of diseases known as myeloproliferative disorders is characterized by overabundance of blood cell lines in peripheral blood. Chronic Myelogenous Leukemia (CML), Primary Myelofibrosis, Chronic Neutrophilic Leukemia Mastocytosis, Essential Thrombocythemia, Polycythemia Vera (PV) and

unclassifiable Myeloproliferative Neoplasms are among the conditions covered by the WHO classification.[1-3]

Most cases of CML are associated with Philadelphia chromosome, t (9:22). Tyrosine kinase activity in protein produced by BCR-ABL fusion gene is thought to be primary cause of chronic phase of CML.[3] JAK2 gene mutation is involved in pathophysiology of PV.[4] Myeloproliferative neoplasms (MPNs) are a group of bone marrow illnesses associated with mutations in JAK2 gene. Megakaryocyte development and proliferation are aided by thrombopoietin receptor protein, which is encoded by MPL gene. Most individuals with Philadelphia chromosome-negative MPNs have somatic mutation in CALR gene. Additionally, PV frequently manifests as an exon 12 mutation.[5,6]

In these conditions, bone marrow histology usually shows hyper cellularity. Reticulin and trichrome stains highlight the fibrosis in myelofibrosis. Although most patients require a bone marrow sample along with cytogenetic testing, this is not always the case. Morphology is still the principal differentiating factor for cancers of the hematopoietic and lymphoid tissues, according to the 2016 WHO categorization system. On the other hand, morphologic diagnoses are increasingly being verified by mutation screening.[7,8]

The yearly incidence of ET is 1.03 per 100,000, PV is 0.84 per 100,000, and primary myelofibrosis is 0.47 per 100,000 for myeloproliferative neoplasms.[9] In a study conducted in Iran among 75 patients, CML was found in (46.7%), myelofibrosis in 29.3%, essential thrombocythemia in 12%, and PV in 12% patients.[10] The rationale of this study was to differentiate several disease subcategories with well-defined clinical and morphological disease patterns among myeloproliferative neoplasms which is of prime importance for early diagnosis and treatment.

Material and Methods

After approval from CPSP [REU: 44876 Dated 24-05-2022], 241 patients fulfilling the inclusion criteria i.e. patients coming to Hematology Department of Jinnah Hospital Lahore for bone marrow biopsy aged 12 – 65 and both males and females were selected. Relapsed patients, patients already on treatment and with incomplete investigations were excluded. Informed written consent was taken from all patients. Sample size of 241 was estimated using WHO calculator with confidence level 95%, 3% margin of error and taking expected prevalence as 6%[11]. Myeloproliferative diseases: (MPD) are characterized by cellular proliferation of one or more blood cell lines in peripheral blood (i.e. Hb >16.5g/dL in males and >16g/dL in females, WBC >12 x 103/µL and platelet count>450x109/L). CML is characterized by increased proliferation of granulocytes >12 x 103/µL without loss of differentiation capacity and diagnosed as positive for BCR/ABL 1 mutation on FISH and Ph-chromosome on cytogenetic analysis. Polycythemia Vera is characterized by Hb >16.5g/dL in males and >16g/dL in females or HCT >49% in men and >48% in females. Essential thrombocythemia is characterized by platelet counts ≥ 450x109/L, iron deficiency anemia (Hb < 10mg/dL). Primary Myelofibrosis shows leucoerythroblastic blood picture with myeloid precursors >1% and nucleated RBCs, > 1/100 white cells on peripheral smear and hyperchromatic bulbous nuclei on bone marrow biopsy. Grade I, II and III fibrosis is seen on Reticulin and trichrome stain. Frequency of myeloproliferative diseases was determined and main clinical and hematologic patterns including B-symptoms; fever (>98.6 F), weight loss (loss of 10% of body weight over 6-month), pallor, visual disturbances, bleeding, hepatomegaly (>14cm), splenomegaly (>12cm), anemia (< 10mg/dL), leukocytosis (>12 x 103/µL), thrombocytopenia (< 150 x109/L) among patients of myeloproliferative neoplasms were noted. All data was recorded on a specially designed demographic proforma. Data analysis was done using SPSS v 26. Quantitative variable like age, duration of disease was presented as mean and standard deviation. Qualitative variables like gender, clinical features and type of MPD were presented as frequency and percentages. Effect modifiers like age and gender were addressed through stratification of data and post stratification chi-square test was used to assess statistical significance with $p \geq 05$.

Results

Age range in this study was from 12 to 65 years with mean age of 38.54 ± 8.65 years. Majority of the patients 172 (71.37%) were between 12 to 40 years of age as shown in Table I. Out of the 241 patients, 175

(72.61%) were male and 66 (27.39%) were females with male to female ratio of 2.7:1. Mean duration of disease was 5.42 ± 2.72 months. In this study, the frequency of myeloproliferative neoplasms in patients presenting for bone marrow biopsy was found to be 76 (31.54%) as shown in Figure I. Frequency of different myeloproliferative neoplasms in patients presenting for bone marrow biopsy were as follows; Chronic myelogenous leukemia in 53, Polycythemia Vera in 13, Essential thrombocythemia in 06 and Primary Myelofibrosis in 04 patients (Table I). Frequency of various clinico-hematological patterns among patients of myeloproliferative neoplasms is shown in Table II i.e. pallor 82.89%, followed by weight loss 80.26%, fever 73.68%, hepatomegaly 32.89%, splenomegaly 19.18%. bleeding 15.79%, and visual disturbance 14.47%. Among hematological parameters, anemia was found in 69.74% leukocytosis in 31.51% and thrombocytopenia in 21.05% patients. Stratification of myeloproliferative neoplasms with respect to age groups and gender found to be insignificant i.e. p-value = 0.492 and p=0.954, respectively as shown in Table III.

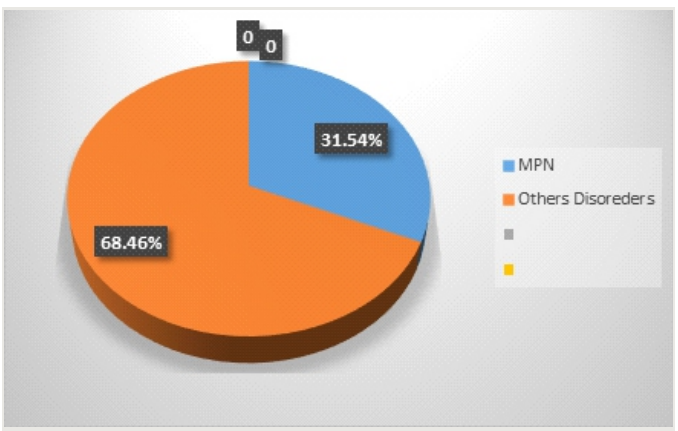

Figure-1: *Frequency of myeloproliferative neoplasms in patients presenting for bone marrow biopsy (n=241).*

Table 1: *Frequency of clinico-hematological patterns among patients of myeloproliferative neoplasms (n=76)*

Different Myeloproliferative Neoplasms	n	Percentage
Chronic myelogenous leukemia	53	69.74
Polycythemia Vera	13	17.11
Essential thrombocythemia	6	7.89
Primary Myelofibrosis	4	5.26
Total	76	100%

Table 2: *Frequency of clinico-hematological patterns among patients of myeloproliferative neoplasms (n=76)*

Clinico-hematological patterns	n	%
Fever	56	73.68
Weight loss	61	80.26
Pallor	63	82.89
Visual disturbances	11	14.47
Bleeding	12	15.79
Hepatomegaly	25	32.89
Splenomegaly	14	19.18
Anemia	53	69.74
Leukocytosis	23	31.51
Thrombocytopenia	16	21.05

Table 3: *Data Stratification*

Groups		Myeloproliferative neoplasms		p- value
		Yes	No	
		n	n	
Age	Dec-40	52	120	0.492
	41-65	24	45	
Gender	Male	55	120	0.954
	Female	21	45	

Discussion

Myeloproliferative neoplasms (MPNs) are distinguished by the aberrant growth of blood cells in the bone marrow. Some diseases, such as essential thrombocythemia, polycythemia vera, and primary myelofibrosis, can have serious side effects and clinical symptoms [2,12]. The lack of knowledge and awareness about MPNs in Pakistan may have an impact on the effectiveness of early diagnosis and therapy. In order to shed light on the prevalence and clinical characteristics of myeloproliferative neoplasms in the local population, this study intends to ascertain the frequency and Clinico-haemtological patterns of these disorders.

Mean age of our study calculation was 38.54 ± 8.65 years, among them 175 (72.61%) were male and 66 (27.39%) were females with male to female ratio of 2.7:1.

Different subtypes of myeloproliferative diseases

occur at different ages. Although MPNs can manifest at any age, some research has concentrated on younger individuals. Studies show that MPNs are typically diagnosed in older people; in fact, up to 20% of patients receive diagnosis before the age of 40[13]. CML typically manifests at young age; 2nd and 3rd decades of life are the most common age group to experience cases, and small percentage in childhood. Although 4-7% of patients with PV are under 40 years old, PV is primarily observed in the elderly. It is commonly recognized that MPNs are more frequent in men. These age trends were similar to our study findings. According to our research, it is in line with a Norwegian study that found the same observation[14], which is further supported by another Swedish study.[15]

In my study, I have found the frequency of myeloproliferative neoplasms in the 241 patients presenting for bone marrow biopsy to be 76 (31.54%). Frequency of different MPNs in patients were as follows; CML in 53 (69.74%), PV in 13(17.1%), ET in 06 (7.89%) and Primary Myelofibrosis in 04 (5.26%) patients. Similar trends were seen in one local study, 49/351 individuals in study were found to have myeloid malignancies. Among them MDS (n=3), MPN (n=3), acute promyelocytic leukemia (n=2), myelomonocytic leukemia (n=1), AML (n=21), CML (n=14), as well as transient abnormal myelopoiesis (n=1). Fever and weight loss were main symptoms at presentation, and most common clinical finding was splenomegaly, followed by pallor, hepatomegaly, and lymphadenopathy. Most frequent laboratory abnormality was anemia, followed by leucocytosis and pancytopenia was observed in 10 patients.[16]

Patients' quality of life is greatly impacted by B symptoms, which are common in MPNs and include fever, weight loss, and night sweats.[7,18] Common complaint among patients with various MPNs is fatigue, which has been found to occur often in those with ET and Pv.[18] Haematological and ophthalmological exams performed in tandem can be used as preventative measure to identify and treat ocular signs of CMPD early and effectively.[19] Patients with PMNs frequently experience ocular consequences as observed in 68.3% higher than our studies observation, such as pain and reduced visual acuity.[20] In one recent study done on 453 (26.2%) in young cluster, including 274 cases of ET, 99 cases of myelofibrosis, followed by 80 cases of PV.[21]

Difference in clinical and hematological findings based on cytogenetics and molecular analysis needs further research.

Conclusion

This study concluded that frequency of myeloproliferative neoplasms in patients presenting for bone marrow biopsy was 31.54% with CML being the most common followed by PV, ET and primary myelofibrosis. Most common clinical presentation was pallor followed by weight loss and fever while most common hemtological abnormality was found to be anemia.

Conflict of Interest *None*

Funding Source *None*

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Authors Contribution

AG, SZ: Conceptualization of Project

ND: Data Collection

AG, SZ: Literature Search

SI: Statistical Analysis

MG: Drafting, Revision

SK: Writing of Manuscript