Correlation of Blood Cell Parameters and Severity of Symptom Burden and Quality of Life Among Individuals with Philadelphia-Negative Myeloproliferative Neoplasia: A Sub-Study of the Filipino MPN-QOL Multicenter Study

Jacqueline Rose E. Agustin, MD,[1] *Flordeluna Z. Mesina, MD*[2]

ABSTRACT

Rationale and Objectives: Individuals with myeloproliferative neoplasia (MPN) have blood cell parameters representing abnormal proliferation of the cell line/lines affected. Considering the implication of symptom burden scores to treatment response and disease progression, with the same implication among changes in blood cell parameters, a question of correlation between the two variables becomes inevitable. This study aims to determine the correlation of controlled blood counts, severity of symptoms and quality of life of individuals with MPN.

Research Design and Methodology: This is a cross-sectional analytical study and a sub-study from the Filipino myeloproliferative neoplasia quality of life (MPN-QOL) multicenter study. Secondary data obtained from the parent study will be used as primary data of this sub-study. Comparative analyses were conducted using Chi-Square Test of Homogeneity or Fisher's Exact Test. Association analysis used Cramer's V coefficient.

Results: Data in this study has shown 52.65 years old as the average age of participants. Most participants had mild symptom burden at 60.53% with the most common symptom being fatigue. Comparative analysis showed the absence of identified statistical difference in the overall symptom burden severity among the three types of MPN.

Discussion and Conclusion: In this study, there was no statistically significant correlation between the severity of symptom burden or quality of life, and the degree of blood count control among the three types of MPN. In practice, controlling hematologic parameters has been a goal to achieve among patients with MPN. This study suggests symptom control and quality of life is not necessarily affected by blood count control.

✉ Jacqueline Rose R. Agustin
jreagustin@gmail.com

[1] Fellow-in-training, Section of Hematology, Department of Internal Medicine, University of Santo Tomas Hospital

[2] Consultant, Section of Hematology, Department of Internal Medicine, University of Santo Tomas Hospital

Academic editor: Leilani B. Mercado-Asis

Submitted date: January 24, 2024

Accepted date: January 25, 2025

Keywords: Myeloproliferative neoplasia, polycythemia vera, essential thrombocythemia, myelofibrosis, blood count control, symptom burden, quality of life

INTRODUCTION

Myeloproliferative neoplasia (MPN) is a group of heterogeneous disorders characterized by abnormal proliferation of one or more terminal myeloid cells.[1] It encompasses the following myeloproliferative diseases: polycythemia vera (PV), essential thrombocytosis (ET) and primary myelofibrosis (PMF). Symptoms vary with each disease entity.[1]

A multinational, multicenter, non-interventional registry (MERGE) was able to collect data showing the prevalence and incidence of MPN in various countries/regions of Asia. Prevalence is at 57-81 per 100,000 hospital patients per year and incidence of 12-15 per 100,000 hospital patients per year over the last four years. Out of the 884 patients who were diagnosed with MPN, 301 had PV, 373 had ET and 169 had MF.[3]

Patients with MPN can be highly symptomatic. PV patients may present with fatigue, headache, visual disturbances and pruritus.[2] Those with ET are often diagnosed incidentally and are mostly asymptomatic.[6] Thirty percent of patients with myelofibrosis are initially asymptomatic, but most would present with symptoms of anemia, splenomegaly and constitutional symptoms. With evolution of the disease process, the symptoms of marrow failure arise. Patients eventually complain of abdominal symptoms such as early satiety, and constitutional symptoms such as weight loss, night sweats and low-grade fever.[8]

An accurate, valid and reliable test, Myeloproliferative Neoplasia Symptom Assessment Form Total Symptom Score (MPN-SAF TSS), has been formulated to effectively quantify symptom burden among individuals with MPN. Increasing total score may indicate disease progression or towards possible leukemic transformation.[10]

Individuals with MPN may have complaints of emotional fatigue and restrictions in social and work activities. The severity of a patient's constitutional symptoms often affects their quality of life. Physicians can monitor this through the use of University of the Philippines-Department of Health Quality of Life (UP-DOH QOL) forms during follow-up.[10] A study by Geyer has identified the prevalence of the 10 symptoms included in the MPN-SAF TSS: fatigue at 87%, concentration problems (62%), early satiety (61%), inactivity (61%), night sweats (53%), itching (53%), abdominal discomfort (52%), bone pain (48%), weight loss (34%) and fever (19%).[9]

Individuals with MPN have blood cell parameters representing abnormal proliferation of the cell line/lines affected. Polycythemia is characterized by trilineage proliferation of cells with elevated levels of hemoglobin and hematocrit to 16.5 g/dL and 45%, respectively as a criterion for diagnosis. ET presents with elevated platelet count of ≥450 x 109/L and PMF has anemia and leukocytosis as its laboratory presentation. As disease progresses or leukemic transformation ensues, changes in blood parameters may occur.[4-8]

The REVEAL study which tried to identify the correlation of symptoms burden and number of controlled blood cell parameters in polycythemic patients showed the absence of significant association between the two variables. The severity of individual symptoms was not affected by blood count control or increasing number of controlled blood count.[2]

Considering the implication of symptom burden scores to treatment response and disease progression, with the same implication among changes in blood cell parameters, a question of correlation between the two variables becomes inevitable. A target in the treatment of MPNs includes bringing of blood counts to normal levels. This study would like to determine the value of achieving controlled blood counts and its association with the severity of symptoms among individuals with MPN.

The Filipino MPN-QOL Multicenter Study was a study which primarily aimed to translate, validate and measure the burden of symptoms and quality of life (QoL) of Filipino MPN patients using the MPN-SAF TSS and UP-DOH QOL for cancer patients, Filipino version. It involved four sites namely: Philippine General Hospital; Jose Reyes Memorial Medical Center; UST Hospital and Makati Medical Center. This is a sub-study from the parent study which aims to correlate the burden of symptoms and quality of life with blood count control among three different Philadelphia-negative MPN.

Table 1. Demographic and clinical profiles of participants according to the type of myeloproliferative neoplasia (N = 167)

Demographic and Clinical Characteristics	Type of Myeloproliferative Neoplasia (N = 167)				Test Statistic a	p-value (Two-Tailed)
	Polycythemia Vera (n = 63, 37.72%)	Essential Thrombocythemia (n = 66, 39.52%)	Myelofibrosis (n = 38, 22.75%)	Total (N = 167)		
Age (Years; $\bar{x}$, SD)	54.03 (13.69)	48.65 (15.37)	57.28 (11.50)	52.65 (14.28)	5.13†	0.007
Sex (f, %)					8.49*	0.014
Male	36 (57.14%)	26 (39.39%)	11 (28.95%)	73 (43.71%)		
Female	27 (42.86%)	40 (60.61%)	27 (71.05%)	94 (56.29%)		
Marital Status (f, %)					3.51	0.752
Single	14 (22.22%)	20 (30.30%)	8 (21.05%)	42 (25.15%)		
Married	39 (61.90%)	39 (59.09%)	27 (71.05%)	105 (62.87%)		
Separated	2 (3.17%)	1 (1.52%)	1 (2.63%)	4 (2.40%)		
Widow/Widower	8 (12.70%)	6 (9.09%)	2 (5.26%)	16 (9.58%)		
Educational Attainment (f, %)					9.95	0.227
Primary Education	3 (4.76%)	5 (8.20%)	1 (2.86%)	9 (5.66%)		
Secondary Education	15 (23.81%)	13 (21.31%)	15 (42.86%)	43 (27.04%)		
Vocational Education	1 (1.59%)	1 (1.64%)	0 (0.00%)	2 (1.26%)		
Tertiary Education	37 (58.73%)	37 (60.66%)	19 (54.29%)	93 (58.49%)		
Post-Graduate Education	7 (11.11%)	5 (8.20%)	0 (0.00%)	12 (7.55%)		
Blood Cell Parameters ($\bar{x}$, SD)						
Hemoglobin (g/dL)	166.51 (26.74)	128.38 (18.91)	112.75 (23.94)	139.21 (32.01)	75.09†	0.001
Hematocrit (%)	47.47 (8.94)	38.78 (4.85)	34.88 (7.91)	41.17 (8.91)	40.81†	0.001
White Blood Cell Count (x109/L)	12.75 (6.46)	12.12 (15.65)	12.48 (9.66)	12.44 (11.51)	0.05	0.953
Platelet (x109/L)	427.63 (208.48)	630.94 (300.47)	457.72 (401.51)	514.83 (310.66)	8.43†	0.001

a Note: Comparative analyses were conducted using Chi-Square Test of Homogeneity or Fisher's Exact Test, Kruskall-Wallis H Test, or One-Way Analysis of Variance (ANOVA)
* Significant at 0.05; † Significant at 0.01;
**Used* with permission from the main study

METHODS

This is a cross-sectional analytical study and a sub-study from the MPN-QOL Multicenter Study. Data collection started from December 2021 to February 2023. The only source of data is the Data Collection Form collected from the main study containing the patients demographic data, CBC result, answered MPN-SAF TSS form and answered by UP-DOH QOL form. The MPN-SAF TSS consists of 10 variables, each scored based on the severity. A maximum score of 10 can be given per variable. An individual score of ≥7 is considered severe, a score of 4 to 6 is considered moderate, a score of 1 to 3 is considered mild and a score of 0 meant no symptoms. The UP-DOH QOL is composed of five domains. A score is given for each domain with a lower score indicating higher QoL.

Statistical analyses were performed using STATA Statistical Software, Version 13, College Station, TX: StataCorp LP. A p-value ≤0.05 was considered statistically significant. Descriptive statistics involved mean and standard deviation for normally-distributed, continuous data; median and interquartile range (IQR) for ordinal and non-normally-distributed, continuous data; and frequency and proportions for categorical data.[17] Comparative analyses were conducted using the Chi-Square Test of Homogeneity

Table 2. Number of controlled blood count parameters according to the type of myeloproliferative neoplasia (N = 167)

Number of Controlled Blood Count Parameters	Type of Myeloproliferative Neoplasia (N = 167)			
	Polycythemia Vera (n = 63)	Essential Thrombocythemia (n = 66)	Myelofibrosis (n = 38)	Total (N = 167)
Uncontrolled	10 (15.87%)	23 (34.85%)	0 (0.00%)	34 (19.76%)
1 Parameter Controlled	31 (49.21%)	36 (54.55%)	2 (5.26%)	69 (41.32%)
2 Parameters Controlled	12 (19.05%)	7 (10.61%)	20 (52.63%)	39 (23.35%)
3 Parameters Controlled	9 (15.87%)	-	12 (31.58%)	21 (13.17%)
4 Parameters Controlled	-	-	4 (10.53%)	4 (2.40%)

* Significant at 0.05
† Significant at 0.01

Table 3. Analyses of the correlations between number of controlled blood count with overall symptom burden severity in polycythemia vera (N = 63)

Overall Symptom Burden Severity	Polycythemia Vera (n = 63)			
	Uncontrolled	1 Parameter Controlled	2 Parameters Controlled	3 Parameters Controlled
No Symptom Burden	5 (27.78%)	5 (29.41%)	0 (0.00%)	0 (0.00%)
Mild Symptom Burden	5 (27.78%)	9 (52.94%)	9 (60.00%)	8 (61.54%)
Moderate Symptom Burden	4 (22.22%)	2 (11.76%)	4 (26.67%)	2 (15.38%)
Severe Symptom Burden	4 (22.22%)	1 (5.88%)	2 (13.33%)	3 (23.08%)
Cramer's V Coefficient			0.269	
p-value (Two-Tailed)			0.136	

* Significant at 0.05
† Significant at 0.01

or Fisher's Exact Test.[17] Finally, association of the number of controlled blood count parameters, overall and specific symptoms burden severity and the QoL among patients with PV, ET and myelofibrosis were individually analyzed using Cramer's V coefficient. [17]

Ethical Considerations

This study was performed in compliance to the following local and international ethical guidelines for research ethics: Declaration of Helsinki 2015, International Conference on Harmonization on Good Clinical Practice (ICH-GCP), Council for International Organizations for Medical Sciences 2016, Good Research Practice (GRP), Philippine National Ethical Guidelines for Health and Health-Related Research of 2017, Philippine Data Privacy Act of 2012 and its Implementing Rules and Regulations (IRR) of 2016. The protocol was reviewed and approved by UST Hospital Research Ethics Committee (USTH-REC).

RESULTS

The study involved 167 participants, 63 diagnosed with PV, 66 had ET and 38 had myelofibrosis. The demographic and clinical characteristics of participants according to the type of MPN are presented in Table 1. In general, the mean age of respondents was 52.65 years. Majority of the participants were also females, married and had a tertiary level education.

The number of controlled blood count parameters among participants was identified according to the type of MPN as illustrated in Table 2. Results showed that regardless of the type of MPN, most participants had at least one blood count parameter controlled

Table 4. Analyses of the correlations between specific symptom burden severity and the number of controlled blood count parameters among patients with polycythemia vera (N = 63)

Specific Symptom Burden Severity	Number of Controlled Blood Count Parameters				p-value
	Uncontrolled	1 Parameter Controlled	2 Parameters Controlled	3 Parameters Controlled	
Fatigue					0.616
No Symptom Burden	2 (20.00%)	3 (9.68%)	2 (16.67%)	1 (10.00%)	
Mild Symptom Burden	7 (70.00%)	14 (45.16%)	4 (33.33%)	5 (50.00%)	
Moderate Symptom Burden	0 (0.00%)	11 (35.48%)	4 (33.33%)	2 (20.00%)	
Severe Symptom Burden	1 (10.00%)	3 (9.68%)	2 (16.67%)	2 (20.00%)	
Early Satiety					0.246
No Symptom Burden	4 (40.00%)	6 (19.35%)	3 (25.00%)	2 (20.00%)	
Mild Symptom Burden	5 (50.00%)	13 (41.94%)	2 (16.67%)	3 (30.00%)	
Moderate Symptom Burden	1 (10.00%)	9 (29.03%)	6 (50.00%)	2 (20.00%)	
Severe Symptom Burden	0 (0.00%)	3 (9.68%)	1 (8.33%)	3 (30.00%)	
Abdominal Discomfort					0.109
No Symptom Burden	8 (80.00%)	7 (22.58%)	6 (50.00%)	4 (40.00%)	
Mild Symptom Burden	2 (20.00%)	13 (41.94%)	3 (25.00%)	4 (40.00%)	
Moderate Symptom Burden	0 (0.00%)	6 (19.35%)	3 (25.00%)	1 (10.00%)	
Severe Symptom Burden	0 (0.00%)	5 (16.13%)	0 (0.00%)	1 (10.00%)	
Inactivity					0.621
No Symptom Burden	5 (50.00%)	8 (25.81%)	2 (16.67%)	3 (30.00%)	
Mild Symptom Burden	4 (40.00%)	10 (32.26%)	4 (33.33%)	3 (30.00%)	
Moderate Symptom Burden	1 (10.00%)	9 (29.03%)	4 (33.33%)	4 (40.00%)	
Severe Symptom Burden	0 (0.00%)	4 (12.90%)	2 (16.67%)	0 (0.00%)	
Problems with Concentration					0.160
No Symptom Burden	5 (50.00%)	9 (29.03%)	6 (50.00%)	1 (10.00%)	
Mild Symptom Burden	5 (50.00%)	10 (32.26%)	3 (25.00%)	6 (60.00%)	
Moderate Symptom Burden	0 (0.00%)	6 (19.35%)	3 (25.00%)	1 (10.00%)	
Severe Symptom Burden	0 (0.00%)	6 (19.35%)	0 (0.00%)	2 (20.00%)	
Night Sweats					0.436
No Symptom Burden	6 (60.00%)	12 (38.71%)	4 (33.33%)	5 (50.00%)	
Mild Symptom Burden	3 (30.00%)	7 (22.58%)	6 (50.00%)	2 (20.00%)	
Moderate Symptom Burden	1 (10.00%)	5 (16.13%)	2 (16.67%)	1 (10.00%)	
Severe Symptom Burden	0 (0.00%)	7 (22.58%)	0 (0.00%)	2 (20.00%)	
Itching or Pruritus					0.282
No Symptom Burden	5 (50.00%)	7 (22.58%)	6 (50.00%)	4 (40.00%)	
Mild Symptom Burden	3 (30.00%)	5 (16.13%)	2 (16.67%)	2 (20.00%)	
Moderate Symptom Burden	2 (20.00%)	12 (38.71%)	1 (8.33%)	1 (10.00%)	
Severe Symptom Burden	0 (0.00%)	7 (22.58%)	3 (25.00%)	3 (30.00%)	
Bone Pain					0.043
No Symptom Burden	7 (70.00%)	9 (29.03%)	8 (66.67%)	1 (10.00%)	
Mild Symptom Burden	1 (10.00%)	10 (32.26%)	2 (16.67%)	6 (60.00%)	
Moderate Symptom Burden	2 (20.00%)	8 (25.81%)	2 (16.67%)	1 (10.00%)	
Severe Symptom Burden	0 (0.00%)	4 (12.90%)	0 (0.00%)	2 (20.00%)	

Table 4. Analyses of the correlations between specific symptom burden severity and the number of controlled blood count parameters among patients with polycythemia vera (N = 63) (continued)

Specific Symptom Burden Severity	Number of Controlled Blood Count Parameters				p-value
	Uncontrolled	1 Parameter Controlled	2 Parameters Controlled	3 Parameters Controlled	
Fever					0.170
No Symptom Burden	0 (100.00%)	21 (67.74%)	10 (83.33%)	10 (100.00%)	
Mild Symptom Burden	0 (0.00%)	8 (25.81%)	1 (8.33%)	0 (0.00%)	
Moderate Symptom Burden	0 (0.00%)	2 (6.45%)	1 (8.33%)	0 (0.00%)	
Severe Symptom Burden	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	
Unintentional Weight Loss					0.102
No Symptom Burden	10 (100.00%)	15 (48.39%)	9 (75.00%)	8 (80.00%)	
Mild Symptom Burden	0 (0.00%)	5 (16.13%)	2 (16.67%)	2 (20.00%)	
Moderate Symptom Burden	0 (0.00%)	7 (22.58%)	1 (8.33%)	0 (0.00%)	
Severe Symptom Burden	0 (0.00%)	4 (12.90%)	0 (0.00%)	0 (0.00%)	

* Significant at 0.05
† Significant at 0.01

Table 5. Analyses of the correlations between number of controlled blood count with overall symptom burden severity in essential thrombocythemia (N = 66)

Overall Symptom Burden Severity	Essential Thrombocythemia (n = 66)		
	Uncontrolled	1 Parameter Controlled	2 Parameters Controlled
No Symptom Burden	3 (17.65%)	12 (70.59%)	2 (11.76%)
Mild Symptom Burden	10 (50.00%)	9 (45.00%)	1 (5.00%)
Moderate Symptom Burden	3 (21.43%)	8 (57.14%)	3 (21.43%)
Severe Symptom Burden	7 (46.67%)	7 (46.67%)	1 (6.67%)
Cramer's V Coefficient		0.243	
p-value (Two-Tailed)		0.254	

* Significant at 0.05
† Significant at 0.01

and only 19.76% had uncontrolled blood count parameters.

Extracted from the main study, the overall symptom burden was mild with most participants complaining of fatigue (38.92%) and inactivity (32.93%). Specifically, symptom burden for fatigue was generally mild for patients with PV and ET and moderate in myelofibrosis. There was no identified statistical difference on the overall symptom burden severity among the three types of MPN. Majority had high QoF (80.24%) with no statistically significant difference when comparing the three MPNs.

Specific analysis of each MPN showed that majority of the symptom burden severity (fatigue, early satiety, abdominal discomfort, inactivity, problems with concentration, night sweats, itching or pruritus, fever and unintentional weight loss) were not statistically correlated. However, it can be noted that bone pain had a statistically significant moderate correlation with the number of controlled blood count parameters in PV. In particular, those with no symptom burden due to bone pain mostly had uncontrolled blood counts.

Specific analyses of the correlations of different specific symptom burden severity with the number of controlled blood count parameters among participants with ET showed that most of the symptom burden severity (fatigue, abdominal discomfort, inactivity,

Table 6. Analyses of the correlation between specific symptom burden severity and number of controlled blood count parameters among patients with essential thrombocythemia (N = 66)

Specific Symptom Burden Severity	Number of Controlled Blood Count Parameters			p-value
	Uncontrolled	1 Parameter Controlled	2 Parameters Controlled	
Fatigue				0.184
No Symptom Burden	1 (4.35%)	5 (13.89%)	3 (42.86%)	
Mild Symptom Burden	11 (47.83%)	12 (33.33%)	1 (14.29%)	
Moderate Symptom Burden	5 (21.74%)	12 (33.33%)	2 (28.57%)	
Severe Symptom Burden	6 (26.09%)	7 (19.44%)	1 (14.29%)	
Early Satiety				0.022
No Symptom Burden	1 (4.35%)	13 (36.11%)	2 (28.57%)	
Mild Symptom Burden	12 (52.17%)	8 (22.22%)	2 (28.57%)	
Moderate Symptom Burden	4 (17.39%)	12 (33.33%)	1 (14.29%)	
Severe Symptom Burden	6 (26.09%)	3 (8.33%)	2 (28.57%)	
Abdominal Discomfort				0.684
No Symptom Burden	5 (21.74%)	15 (41.67%)	3 (42.86%)	
Mild Symptom Burden	12 (52.17%)	11 (30.56%)	2 (28.57%)	
Moderate Symptom Burden	0 (0.00%)	8 (22.22%)	2 (28.57%)	
Severe Symptom Burden	6 (26.09%)	2 (5.56%)	0 (0.00%)	
Inactivity				0.275
No Symptom Burden	6 (26.09%)	14 (38.89%)	2 (28.57%)	
Mild Symptom Burden	11 (47.83%)	11 (30.56%)	1 (14.29%)	
Moderate Symptom Burden	2 (8.70%)	7 (19.44%)	1 (14.29%)	
Severe Symptom Burden	4 (17.39%)	4 (11.11%)	3 (42.86%)	
Problems with Concentration				
No Symptom Burden	3 (13.04%)	16 (44.44%)	3 (42.86%)	0.327
Mild Symptom Burden	10 (43.48%)	12 (33.33%)	2 (28.57%)	
Moderate Symptom Burden	6 (26.09%)	4 (11.11%)	1 (14.29%)	
Severe Symptom Burden	4 (17.39%)	4 (11.11%)	1 (14.29%)	
Night Sweats				0.780
No Symptom Burden	10 (43.48%)	18 (50.00%)	2 (28.57%)	
Mild Symptom Burden	7 (30.43%)	11 (30.56%)	4 (57.14%)	
Moderate Symptom Burden	3 (13.04%)	4 (11.11%)	0 (0.00%)	
Severe Symptom Burden	3 (13.04%)	3 (8.33%)	1 (14.29%)	
Itching or Pruritus				0.270
No Symptom Burden	8 (34.78%)	18 (50.00%)	5 (71.43%)	
Mild Symptom Burden	9 (39.13%)	13 (36.11%)	1 (14.29%)	
Moderate Symptom Burden	2 (8.70%)	3 (8.33%)	0 (0.00%)	
Severe Symptom Burden	4 (17.39%)	2 (5.56%)	1 (14.29%)	
Bone Pain				0.755
No Symptom Burden	7 (30.43%)	16 (44.44%)	4 (57.14%)	
Mild Symptom Burden	8 (34.78%)	12 (33.33%)	2 (28.57%)	
Moderate Symptom Burden	4 (17.39%)	3 (8.33%)	1 (14.29%)	
Severe Symptom Burden	4 (17.39%)	5 (13.89%)	0 (0.00%)	

Table 6. Analyses of the correlation between specific symptom burden severity and number of controlled blood count parameters among patients with essential thrombocythemia (N = 66) (continued)

Specific Symptom Burden Severity	Number of Controlled Blood Count Parameters			p-value
	Uncontrolled	1 Parameter Controlled	2 Parameters Controlled	
Fever				0.334
No Symptom Burden	17 (73.91%)	29 (80.56%)	6 (85.71%)	
Mild Symptom Burden	3 (13.04%)	5 (13.89%)	1 (14.29%)	
Moderate Symptom Burden	3 (13.04%)	2 (5.56%)	0 (0.00%)	
Severe Symptom Burden	0 (0.00%)	0 (0.00%)	0 (0.00%)	
Unintentional Weight Loss				0.431
No Symptom Burden	12 (52.17%)	26 (72.22%)	1 (50.00%)	
Mild Symptom Burden	6 (26.09%)	7 (19.44%)	1 (50.00%)	
Moderate Symptom Burden	3 (13.04%)	1 (2.78%)	0 (0.00%)	
Severe Symptom Burden	2 (8.70%)	2 (5.56%)	0 (0.00%)	

* Significant at 0.05
† Significant at 0.01

Table 7. Analyses of the correlations between number of controlled blood count with overall symptom burden severity in myelofibrosis (N = 38)

Overall Symptom Burden Severity	Myelofibrosis (n = 38)				
	Uncontrolled	1 Parameter Controlled	2 Parameters Controlled	3 Parameters Controlled	4 Parameters Controlled
No Symptom Burden	0 (0.00%)	0 (0.00%)	1 (20.00%)	4 (80.00%)	0 (0.00%)
Mild Symptom Burden	0 (0.00%)	0 (0.00%)	6 (85.71%)	0 (0.00%)	1 (14.29%)
Moderate Symptom Burden	0 (0.00%)	1 (7.69%)	8 (61.54%)	3 (23.08%)	1 (7.69%)
Severe Symptom Burden	0 (0.00%)	1 (7.69%)	5 (38.46%)	5 (38.46%)	2 (15.38%)
Cramer's V Coefficient			0.318		
p-value (Two-Tailed)			0.242		

* Significant at 0.05
† Significant at 0.01

problems with concentration, night sweats, itching or pruritus, bone pain, fever and unintentional weight loss) were not statistically correlated. Nevertheless, results indicated a statistically significant, moderate correlation between symptom burden severity due to early satiety and the number of controlled blood count parameters. This result showed that most patients with controlled blood count parameters had no symptom burden while those with uncontrolled blood count parameters complained of severe symptom burden.

In myelofibrosis, the severity of the following symptoms (fatigue, abdominal discomfort, inactivity, problems with concentration, night sweats, bone pain and unintentional weight loss) were not statistically correlated with the number of controlled blood count. Nonetheless, results showed statistically significant associations for early satiety, itching or pruritus, and fever. A higher number of controlled blood count parameters lead to more severe symptom burden for early satiety, but lower symptom burden for pruritus and fever.

Correlation analyses in Table 9 indicated that the coefficients for correlation of the number of controlled blood count parameters and global QoL among those with PV, ET and myelofibrosis are considered moderate correlation coefficients but these correlations were not statistically significant.

DISCUSSION

MPN encompasses disease processes in the spectrum of clonal myeloid diseases. This is a disease diagnosed among patients ≥50 years of age congruent with the data which shows 52.65 years old as the average age of participants.

Table 8. Analyses of the correlation between specific symptom burden severity and number of controlled blood count parameters among patients with myelofibrosis (N = 38)

Specific Symptom Burden Severity	Number of Controlled Blood Count Parameters				p-value
	1 Parameter Controlled	2 Parameters Controlled	3 Parameters Controlled	4 Parameters Controlled	
Fatigue					0.833
No Symptom Burden	0 (0.00%)	4 (20.00%)	2 (16.67%)	0 (0.00%)	
Mild Symptom Burden	0 (0.00%)	6 (30.00%)	3 (25.00%)	2 (50.00%)	
Moderate Symptom Burden	1 (50.00%)	8 (40.00%)	4 (33.33%)	1 (25.00%)	
Severe Symptom Burden	1 (50.00%)	2 (10.00%)	3 (25.00%)	1 (25.00%)	
Early Satiety					0.020
No Symptom Burden	0 (0.00%)	6 (30.00%)	2 (16.67%)	0 (0.00%)	
Mild Symptom Burden	0 (0.00%)	3 (15.00%)	2 (16.67%)	0 (0.00%)	
Moderate Symptom Burden	1 (50.00%)	7 (35.00%)	7 (58.33%)	3 (75.00%)	
Severe Symptom Burden	1 (50.00%)	4 (20.00%)	1 (8.33%)	1 (25.00%)	
Abdominal Discomfort					0.165
No Symptom Burden	0 (0.00%)	10 (50.00%)	2 (16.67%)	1 (25.00%)	
Mild Symptom Burden	0 (0.00%)	2 (10.00%)	4 (33.33%)	2 (50.00%)	
Moderate Symptom Burden	2 (100.00%)	7 (35.00%)	5 (41.67%)	0 (0.00%)	
Severe Symptom Burden	0 (0.00%)	1 (5.00%)	1 (8.33%)	1 (25.00%)	
Inactivity					0.301
No Symptom Burden	0 (0.00%)	7 (35.00%)	3 (25.00%)	0 (0.00%)	
Mild Symptom Burden	0 (0.00%)	7 (35.00%)	2 (16.67%)	2 (50.00%)	
Moderate Symptom Burden	2 (100.00%)	3 (15.00%)	5 (41.67%)	1 (25.00%)	
Severe Symptom Burden	0 (0.00%)	3 (15.00%)	2 (16.67%)	1 (25.00%)	
Problems with Concentration					0.829
No Symptom Burden	0 (0.00%)	11 (55.00%)	4 (33.33%)	1 (25.00%)	
Mild Symptom Burden	1 (50.00%)	4 (20.00%)	3 (25.00%)	1 (25.00%)	
Moderate Symptom Burden	1 (50.00%)	3 (15.00%)	3 (25.00%)	1 (25.00%)	
Severe Symptom Burden	0 (0.00%)	2 (10.00%)	2 (16.67%)	1 (25.00%)	
Night Sweats					0.515
No Symptom Burden	1 (50.00%)	11 (55.00%)	5 (41.67%)	1 (25.00%)	
Mild Symptom Burden	0 (0.00%)	6 (30.00%)	2 (16.67%)	2 (50.00%)	
Moderate Symptom Burden	0 (0.00%)	3 (15.00%)	2 (16.67%)	1 (25.00%)	
Severe Symptom Burden	1 (50.00%)	0 (0.00%)	3 (25.00%)	0 (0.00%)	
Itching or Pruritus					0.045
No Symptom Burden	1 (50.00%)	6 (30.00%)	9 (75.00%)	3 (75.00%)	
Mild Symptom Burden	1 (50.00%)	6 (30.00%)	1 (8.33%)	1 (25.00%)	
Moderate Symptom Burden	0 (0.00%)	0 (0.00%)	2 (16.67%)	0 (0.00%)	
Severe Symptom Burden	0 (0.00%)	8 (40.00%)	0 (0.00%)	0 (0.00%)	
Bone Pain					0.778
No Symptom Burden	0 (0.00%)	2 (10.00%)	5 (41.67%)	0 (0.00%)	
Mild Symptom Burden	1 (50.00%)	7 (35.00%)	1 (8.33%)	1 (25.00%)	
Moderate Symptom Burden	0 (0.00%)	5 (25.00%)	4 (33.33%)	2 (50.00%)	

Table 8. Analyses of the correlation between specific symptom burden severity and number of controlled blood count parameters among patients with myelofibrosis (N = 38) (continued)

Specific Symptom Burden Severity	Number of Controlled Blood Count Parameters				p-value
	1 Parameter Controlled	2 Parameters Controlled	3 Parameters Controlled	4 Parameters Controlled	
Severe Symptom Burden	1 (50.00%)	6 (30.00%)	2 (16.67%)	1 (25.00%)	
Fever					0.008
No Symptom Burden	1 (50.00%)	16 (80.00%)	12 (100.00%)	4 (100.00%)	
Mild Symptom Burden	0 (0.00%)	2 (10.00%)	0 (0.00%)	0 (0.00%)	
Moderate Symptom Burden	0 (0.00%)	2 (10.00%)	0 (0.00%)	0 (0.00%)	
Severe Symptom Burden	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	
Unintentional Weight Loss					0.162
No Symptom Burden	0 (0.00%)	8 (40.00%)	9 (75.00%)	2 (50.00%)	
Mild Symptom Burden	1 (50.00%)	4 (20.00%)	1 (8.33%)	0 (0.00%)	
Moderate Symptom Burden	1 (50.00%)	3 (15.00%)	2 (16.67%)	2 (50.00%)	
Severe Symptom Burden	0 (0.00%)	5 (25.00%)	0 (0.00%)	0 (0.00%)	

* Significant at 0.05
† Significant at 0.01

Table 9. Analyses of the correlation between the number of controlled blood count with quality of life according to the type of myeloproliferative neoplasia (N = 167)

Number of Controlled Blood Count Parameters	Polycythemia Vera (n = 63)		Essential Thrombocythemia (n = 66)		Myelofibrosis (n = 38)	
	Moderate	High	Moderate	High	Moderate	High
Uncontrolled	1 (7.69%)	10 (20.00%)	7 (63.64%)	16 (29.09%)	0 (0.00%)	0 (0.00%)
1 Parameter Controlled	9 (69.23%)	22 (44.00%)	3 (27.27%)	33 (60.00%)	1 (11.11%)	1 (3.45%)
2 Parameters Controlled	1 (7.69%)	11 (22.00%)	1 (9.09%)	6 (10.91%)	7 (77.78%)	13 (44.83%)
3 Parameters Controlled	2 (15.38%)	7 (14.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	12 (41.38%)
4 Parameters Controlled	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	3 (10.34%)
Cramer's V Coefficient	0.231		0.274		0.394	
p-value (Two-Tailed)	0.340		0.083		0.116	

a Note: Comparative analyses were conducted using the Chi-Square Test of Homogeneity or Fisher's Exact Test, Kruskal-Wallis H Test, or One-Way Analysis of Variance (ANOVA)
* Significant at 0.05
† Significant at 0.01

Blood count control was based on hematologic criteria adapted from the International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) response criteria and participants were categorized depending on the number of blood cell parameters they have under control. In this study, most patients had at least one blood count parameter controlled, regardless of the type of MPN and only 19.76% had all blood parameters uncontrolled. Most of the participants with PV had one out of three parameters controlled. Most patients with ET had at least one of two

parameters controlled and majority of participants with myelofibrosis had two out of four hematologic criteria controlled.

Patients with MFN can be asymptomatic upon diagnosis and are only identified due to blood count abnormalities. There are, however, individuals who may present with persistent symptoms. The five most common patient-reported symptoms are fatigue, early satiety, inactivity, pruritus and problems with concentration.[2]

In this study, most participants had mild symptom burden at 60.53% regardless of the type of MPN, with the most common symptom being fatigue at 38.92%. Participants with PV and ET had mild symptom burden due to fatigue, while those with myelofibrosis complained of moderate symptom burden due to fatigue, early satiety and abdominal discomfort. This is congruent with the findings of Grunwald (2019) which showed that 80% of patients with MPN may experience high persistence of fatigue with at least mild severity.[2] A study by Scherber (2016) showed fatigue to be prevalent among their 1,788 respondents with MPN with degree of severity associated with higher body mass index, alcohol use and tobacco use.[22]

Comparative analysis showed the absence of identified statistical difference in overall symptom burden severity among the three types of MPN. It is, however, of note that upon analysis of specific symptoms, a significantly higher proportion of participants with PV have moderate symptom burden due to itching or pruritus congruent with estimated prevalence of PV-associated pruritus at 31%-69% making it one of the main features of PV.[24]

A part of the outcomes of the study correlated symptom burden with number of controlled blood count parameters based on the control criteria. In this study, there was no statistically significant correlation between severity of symptom burden and degree of blood count control among the three types of MPN. This is congruent with the REVEAL study which did not show a significant association between the symptom score among polycythemic patients and exact number of blood count controlled (1, 2, 3, or no counts controlled). The severity of individual symptoms was not affected by blood count control or increasing number of controlled blood count.[2] There are no current studies which correlated blood count control and symptom burden for patients with ET and myelofibrosis.

Analysis of each MPN showed some statistically significant findings. Participants with PV with uncontrolled blood counts had no bone pains. Those with ET with uncontrolled blood counts had early satiety as a severe symptom burden. More severe symptom burden on early satiety was associated with higher degree of blood count control. Fever and pruritus on the other hand had a lower symptom burden, but with a higher number of blood parameters controlled.

Symptom burden often affect the QoL. The presence of symptoms caused these patients emotional hardship, interference and limitation in daily activities and interference with patient and family social life.[11] In this study, however, 80.24% had high QoL and none reported having a low QoL. There was no statistically significant correlation seen with participants' QoL and blood count control.

CONCLUSION

In clinical practice, controlling hematologic parameters has been a goal that healthcare providers try to achieve in patients with MPN. A certain degree of blood counts have been set as criteria for complete response to therapy. This study suggests symptom control and QoL is not necessarily affected by blood count control and had no clear association with the degree of blood count control.

This study highlights the significance of regular monitoring of symptom burden and patients QoL rather than focusing and relying on controlling blood count levels to define the degree of disease control.

RECOMMENDATIONS

This study can be used as a reference for future studies on symptom burden and QoL among Filipino MPN patients. A limitation of this study is that this is cross-sectional which obtained data at a single point in time. Symptoms and blood counts tend to be more dynamic with treatment. A prospective study following the symptom burden, QoL and degree of blood count control of patients with MPN and a higher number of populations could provide more significant findings.

REFERENCES

1. Wilkins BS. Myeloproliferative neoplasms. *Diagn Histopathol (Oxf)* [Internet]. 2021;27(9):373–9. Available from: http://dx.doi.org/10.1016/j.mpdhp.2021.06.003
2. Grunwald MR, Burke JM, Kuter DJ, Gerds AT, Stein B, Walshauser MA, et al. Symptom burden and blood counts in patients with polycythemia vera in the United States: An analysis from the REVEAL study. *Clin Lymphoma Myeloma Leuk* [Internet]. 2019;19(9):579-584.e1. Available from: http://dx.doi.org/10.1016/j.clml.2019.06.001
3. Yassin MA, Taher A, Mathews V, Hou H-A, Shamsi T, Tuğlular TF, et al. MERGE: A multinational, multicenter observational registry for myeloproliferative neoplasms in Asia, including Middle East, Turkey, and Algeria. *Cancer Med* [Internet]. 2020;9(13):4512–26. Available from: http://dx.doi.org/10.1002/cam4.3004
4. Iurlo A, Cattaneo D, Bucelli C, Baldini L. New perspectives on polycythemia vera: From diagnosis to therapy. *Int J Mol Sci* [Internet]. 2020;21(16):5805. Available from: http://dx.doi.org/10.3390/ijms21165805
5. Ashorobi D, Gohari P. Essential thrombocytosis. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
6. Rumi E, Cazzola M. How I treat essential thrombocythemia. *Blood* [Internet]. 2016;128(20):2403–14. Available from: http://dx.doi.org/10.1182/blood-2016-05-643346
7. Tefferi A. Primary myelofibrosis: 2021 update on diagnosis, risk-stratification and management. *Am J Hematol* [Internet]. 2021;96(1):145–62. Available from: http://dx.doi.org/10.1002/ajh.26050
8. Cervantes F. How I treat myelofibrosis. *Blood* [Internet]. 2014;124(17):2635–42. Available from: http://dx.doi.org/10.1182/blood-2014-07-575373
9. Geyer H, Mesa RA. Approach to MPN symptom assessment. *Curr Hematol Malig Rep* [Internet]. 2017;12(5):381–8. Available from: http://dx.doi.org/10.1007/s11899-017-0399-5
10. Emanuel RM, Dueck AC, Geyer HL, Kiladjian J-J, Slot S, Zweegman S, et al. Myeloproliferative neoplasm (MPN) symptom assessment form total symptom score: prospective international assessment of an abbreviated symptom burden scoring system among patients with MPNs. *J Clin Oncol* [Internet]. 2012;30(33):4098–103. Available from: http://dx.doi.org/10.1200/JCO.2012.42.3863
11. Ting FI, Callueng JM, Vallente J, Hurtado RA, Ramirez A, Catedral LI, et al. Assessing the quality of life of Filipino cancer patients: A survey of Filipino oncologists. *Asian J Oncol* [Internet]. 2020;6(01):20–8. Available from: http://dx.doi.org/10.1055/s-0040-1703420
12. Harrison CN, Koschmieder S, Foltz L, Guglielmelli P, Flindt T, Koehler M, et al. The impact of myeloproliferative neoplasms (MPNs) on patient quality of life and productivity: results from the international MPN landmark survey. *Ann Hematol* [Internet]. 2017;96(10):1653–65. Available from: http://dx.doi.org/10.1007/s00277-017-3082-y
13. Spivak JL. How I treat polycythemia vera. *Blood* [Internet]. 2019;134(4):341–52. Available from: http://dx.doi.org/10.1182/blood.2018834044
14. Campbell PJ, MacLean C, Beer PA, Buck G, Wheatley K, Kiladjian J-J, et al. Correlation of blood counts with vascular complications in essential thrombocythemia: analysis of the prospective PT1 cohort. *Blood* [Internet]. 2012;120(7):1409–11. Available from: http://dx.doi.org/10.1182/blood-2012-04-424911
15. Buxhofer-Ausch V, Steurer M, Sormann S, Schloegl E, Schimetta W, Gisslinger B, et al. Impact of white blood cells on thrombotic risk in patients with optimized platelet count in essential thrombocythemia. *Eur J Haematol* [Internet]. 2018;131–5. Available from: http://dx.doi.org/10.1111/ejh.13070
16. Tefferi A, Cervantes F, Mesa R, Passamonti F, Verstovsek S, Vannucchi AM, et al. Revised response criteria for myelofibrosis: International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) and European LeukemiaNet (ELN) consensus report. *Blood* [Internet]. 2013;122(8):1395–8. Available from: http://dx.doi.org/10.1182/blood-2013-03-488098
17. Daniel WW, Cross CL. Biostatistics: A Foundation for Analysis in the Health Sciences. 10th ed. New Jersey, USA: Wiley; 2013.
18. Allen M. The SAGE encyclopedia of communication research methods [Internet]. 2455 Teller Road, Thousand Oaks California 91320: SAGE Publications, Inc; 2017. Available from: http://dx.doi.org/10.4135/9781483381411
19. Lautert L. Professional fatigue: empirical study with hospital nurses. *Rev Gaucha Enferm*. 1997;18(2):133–44.
20. Pera G, Serra-Prat M. Burnout syndrome: prevalence and associated factors among workers in a district hospital. *Gac Sanit* [Internet]. 2002;16(6):480–86. Available from: http://dx.doi.org/10.1016/s0213-9111(02)71968-7
21. Ruste SA, Ngelangel C. QoL of colorectal cancer stoma patients at the Philippine General Hospital - Cancer Institute. *Philippine Journal of Internal Medicine*. 2011;49(1):38–41.
22. Barosi G, Mesa R, Finazzi G, Harrison C, Kiladjian J-J, Lengfelder E, et al. Revised response criteria for polycythemia vera and essential thrombocythemia: an ELN and IWG-MRT consensus project. *Blood* [Internet]. 2013;121(23):4778–81. Available from: http://dx.doi.org/10.1182/blood-2013-01-478891
23. Scherber RM, Kosiorek HE, Senyak Z, Dueck AC, Clark MM, Boxer MA, et al. Comprehensively understanding fatigue in patients with myeloproliferative neoplasms: Myeloproliferative neoplasm fatigue. *Cancer* [Internet]. 2016;122(3):477–85. Available from: http://dx.doi.org/10.1002/cncr.29753
24. Lelonek E, Matusiak Ł, Wróbel T, Szepietowski JC. Aquagenic pruritus in polycythemia vera: Clinical characteristics. *Acta Derm Venereol* [Internet]. 2018;98(5):496–500. Available from: http://dx.doi.org/10.2340/00015555-2906