



Research Article

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EVALUATION OF PROGNOSIS, MORTALITY AND PLATELET INDEXES, PLATELET/LYMPHOCYTE AND NEUTROPHIL/LYMPHOCYTE RATIOS OF PALLIATIVE CARE PATIENTS

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Abstract

Objectives: In this study, it was aimed to evaluate the clinical significance of platelet indices, platelet, neutrophil, and lymphocyte values, as well as neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR) values and their relationship with mortality in palliative care patients.

Materials and Methods: The data of 464 patients in the palliative care service were analyzed retrospectively. Sociodemographic characteristics of the patients, diagnosis, length of stay in the service, the way they were admitted to the palliative service and the way they were discharged from the palliative service, hospitalization and hematological parameters were recorded.

Results: The mean age of the 464 patients included in the study was 75.15 ± 13.63 years. It was seen that 68.30% of the patients were alive during the time period they were included in the study. When the admission and discharge blood values of the patients who died and the patients who survived were compared, the WBC and neutrophil values of the patients who died were found to be higher than the patients who survived, while the platelet and lymphocyte values of the patients who died were found to be lower. While admission and discharge NLR values, admission PLR values, discharge MPV values and discharge PDW values were found to be significantly higher in patients who died than in patients who survived, discharge PCT value was found low.

Conclusion: Leukocytosis, thrombocytopenia, lymphopenia, and neutrophilia were dominant in the hematological parameters of the patients who died compared to the patients who survived. In contrast, the admission PLR value was found to be higher in patients who died than the patients who survived.

Keywords: Palliative care, prognosis, mortality.

Introduction

Palliative care is a multidisciplinary approach that aims to achieve a good quality of life by preventing or alleviating the physical, psychosocial, and spiritual distress of patients who face problems caused by life-threatening diseases through early detection and comprehensive evaluation.¹ Today, it is known that patients with neurological diseases and advanced cancer need palliative care with a well-coordinated team to determine their needs and provide effective care.²

Neutrophilia, lymphopenia, and thrombocytopenia in peripheral blood are evaluated as responses to systemic inflammation.^{3,4} In recent years, the relationship of neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR) and mean platelet volume (MPV) obtained from routine complete blood count with various diseases and their effects on mortality in critically ill patients especially cancer patients, have been investigated and valuable results have been obtained.⁵⁻⁸ In a study investigating the prognostic importance of platelet indices performed in a mixed intensive care unit, it was concluded that MPV and platelet distribution width (PDW) values were positively correlated with disease severity and negatively correlated with platelet count and that PDW and PCT values were prognostic biomarkers defining disease severity, such as platelet level.³ Senyurt et al.⁹, in their study on patients hospitalized in an intensive care Unit, found a significant difference in hemogram parameters (MPV, RDW, NLR, PLO) between deceased patients and survivors. They observed that the discriminating power of the hemogram parameters for mortality was higher than SOFA (Sequential Organ Failure Assessment), APACHE II (Acute Physiology and Chronic Health Evaluation) scores, and CRP (C-Reactive Protein). These parameters can be obtained or calculated automatically with complete blood count devices at low cost and have advantages such as rapid decision-making in critically ill patients and initiation of appropriate treatment.

In our study, it was aimed to evaluate the clinical importance of routinely studied platelet indices (PCT, MPV, PDW), platelet, neutrophil, and lymphocyte values, as well as easily calculated NLR and PLR values, and their relationship with mortality in palliative care patients who are exposed to many factors that may affect hematological parameters.

Materials and Methods

This study was designed as a retrospective, cross-sectional and analytical study. It was conducted with the data obtained by retrospectively scanning a total of 495 patients who were hospitalized in the Palliative Care Service of the local University Training and Research Hospital. The examinations and information to be used in the study were obtained from the records of the hospital. If the same patient had more than one admission during

this period, the first hospitalization data were included in the study. Thirty-one of 495 patients were excluded from the study due to missing data, and the data of 464 patients were evaluated in the study.

The data of the patients were evaluated retrospectively. Sociodemographic characteristics such as age, gender and marital status of the patients, diagnosis/pre-diagnosis, length of stay in the service, the way of being admitted to the palliative service (emergency, outpatient clinic, intensive care, other services) and the way of discharge from the palliative service (intensive care transfer/referral, Transfer/transfer to other services, discharged with recovery, death), hospitalization and discharge hematological parameters were studied and recorded. Hematological parameters such as thrombocyte indices (MPV, PDW, PCT), leukocytes, lymphocytes, neutrophils, thrombocytes, NLR and PLR values were recorded.

Statistical Analyses

The obtained data were analyzed with SPSS (Statistical Package for the Social Sciences) 21 package program. The numerical data were evaluated using descriptive statistics (number, percentage, mean, standard deviation). Mann-Whitney U test was used for comparisons between groups when the data were not normally distributed. Chi-Square analysis and Correlation analysis were used for the relationship and/or dependency between the variables. It was stated if there was a significant difference if the level of significance was $p < 0.05$.

Results

In our study, 464 patients admitted to the Palliative Service of the local University Training and Research Hospital were included. In the study, 58.84% of the patients were male, 52.62% were married, and the mean age was 75.15 ± 13.63 years. The mean length of stay in the hospital of the patients in the palliative service was 22.62 ± 23.51 days.

The patients in our study had at least one chronic disease. In the study, 70.32% of them had hypertension, 68.52% neurological diseases and 50.61% cardiovascular diseases. Oral intake disorder was present in 56.32% of the patients, and pressure ulcer was present in 42.53% of the patients. In the study, 41.82% of the patients were sent from family medicine outpatient clinics and other outpatient clinics. When the discharge status from the service was examined, it was found that 59.91% of them were discharged with recovery. It was found that 57 (90.50%) of 63 patients transferred to the intensive care unit died during intensive care therapy. It was observed that 68.30% of the 464 patients were alive, and 31.70% died in the period they were included in the study (Table 1).

Table 1. Sociodemographic, clinical characteristics, hospitalization, and mortality rates of the patients

Variables	n	%
Gender		
Female	191	41.16
Male	273	58.84
Marital status		
Single	29	6.32
Married	244	52.62
Not mentioned	191	41.16
Chronic diseases		
Diabetes mellitus	128	27.61
Hypertension	326	70.32
Cardiovascular disease	235	50.61
Neurological disease	318	68.52
Malignancy	134	28.91
Pulmonary disease	232	50.00
Pressure ulcer	197	42.53
Oral feeding disorder	261	56.32
Units that referred patients to the palliative service		
Family medicine clinic	194	41.82
Emergency clinic	129	27.82
Intensive care unit	100	21.63
Other services	41	8.82
Discharge from palliative care		
Discharge with recovery	278	59.91
Transfer to an intensive care unit	63	13.62
Transfer to other services	33	7.13
Death	90	19.42
Survival status of patients who were sent to an intensive care unit		
Died	57	90.50
Survived	6	9.50
Total	63	100
Mortality status		
Survived	317	68.30
Died	147	31.70
Total	464	100

(n: number)

There was a statistically significant no difference between the patients' mortality status and age ($p=0.495$), length of stay in the service ($p=0.319$), gender ($p=0.054$), and marital status ($p=0.349$), and the unit that admitted to palliative service ($p=0.086$). The mortality rate was numerically higher in males (35.24%), aged 51-60 (42.92%), married (34.43%), and patients sent from the emergency department (39.51%).

In our study, the mortality rate of patients with malignancy and without neurological disease was found to be statistically significantly higher ($p<0.001$) (Table 2).

Table 2. Comparison of Mortality Status of Patients According to Concomitant Diseases

Concomitant Diseases		Survived		Died		Total	p
		n	%	n	%	n	
Diabetes Mellitus	No	229	68.18	107	31.82	336	0.902
	Yes	88	68.82	40	31.18	128	
Hypertension	No	92	66.71	46	33.29	138	0.619
	Yes	225	69.09	101	31.01	326	
Cardiovascular disease	No	159	69.39	70	30.61	229	0.611
	Yes	158	67.28	77	32.72	235	
Neurological disease	No	75	51.44	71	48.56	146	<0.001
	Yes	242	76.17	76	23.83	318	
Malignancy	No	257	77.91	73	22.09	330	<0.001
	Yes	60	44.82	74	55.18	134	
Pulmonary disease	No	153	65.88	79	34.12	232	0.272
	Yes	164	70.73	68	29.27	232	
Total		317	68.30	147	31.70	464	

In our study, the hematological parameters of the patients in the first blood tests taken at the time of admission to the hospital were recorded as the first results, and the hematological parameters in the last blood tests before discharge from the service (death, discharge, transfer) were recorded as the second results. There was no significant difference between the age and gender of the patients in terms of hospitalization and hematological parameters at discharge.

The comparison of the first and second hematological parameters (PLR, NLR, MPV) of the patients according to the comorbid conditions is given in Table 3.

Accordingly, the mean values of 1. PLR, 1. NLR, and 2. NLR were found to be statistically significantly lower in patients with diabetes mellitus than in patients without diabetes mellitus. The mean values of 1. PLR, 1. NLR, and 2. NLR were statistically significantly lower and 1. MPV mean values were higher in neurological patients compared to those without. The mean values of 1. PLR, 2. PLR, 1. NLR and 2. NLR were statistically higher and 1. MPV mean values were lower in patients with malignancy compared to those without. The mean values of 1. PLR, 1. NLR, 2. NLR were statistically significantly lower and 2. MPV mean values were higher in patients with pressure ulcers compared to those without. (Table 3). When admission and discharge hematological parameters of the patients were compared, it was seen that the 1. PLR value was statistically significantly higher than the 2. PLR value. There was no significant difference between admission and discharge results in other parameters.

When hospitalization and discharge, hematological parameters were compared according to the survival status of the patients, the mean values of the 2. WBC, 2. Neutrophil, 2. Lymphocyte, 2. MPV, 1. PLR, 2. NLR, 2. MPV, and

2. PDW of the deceased patients was found to be significantly higher and 2. Platelet and 2. PCT values were found to be significantly lower compared to the patients who survived (Table 4).

Table 3. Comparison of Patients' Diseases and PLR, NLR, MPV Values

Variables		DM	HT-CRD	KVD	ND	Malignancy	PD	Pressure ulcer
1. P L R	No	268.83 ± 209.78	256.14 ± 223.46	262.75 ± 206.46	289.72 ± 233.61	232.24 ± 154.01	253.52 ± 208.88	270.43 ± 204.47
	Yes	221.26 ± 151.38	255.52 ± 184.15	248.85 ± 186.30	240.09 ± 174.95	313.51 ± 266.26	257.89 ± 183.53	235.74 ± 183.58
	P	0.014	0.575	0.383	0.034	0.002	0.372	0.021
2. P L R	No	250.31 ± 219.07	250.10 ± 227.05	261.29 ± 235.67	284.47 ± 288.29	217.85 ± 161.95	245.61 ± 239.75	269.81 ± 247.67
	Yes	235.76 ± 212.89	244.68 ± 213.31	231.69 ± 197.09	228.77 ± 173.04	316.34 ± 304.11	246.98 ± 192.67	214.43 ± 162.71
	P	0.126	0.872	0.268	0.651	0.039	0.093	0.052
1. N L R	No	9.43 ± 11.65	8.72 ± 10.54	9.05 ± 9.97	10.56 ± 10.81	7.42 ± 7.87	8.82 ± 10.19	9.47 ± 10.47
	Yes	7.51 ± 8.13	8.98 ± 10.95	8.76 ± 11.60	8.14 ± 10.75	12.56 ± 15.33	8.98 ± 11.43	8.13 ± 11.25
	P	0.022	0.473	0.241	<0.001	<0.001	0.582	0.006
2. N L R	No	14.70 ± 76.85	9.68 ± 11.13	12.20 ± 19.20	22.70 ± 115.52	12.57 ± 77.64	10.51 ± 16.54	17.51 ± 86.52
	Yes	9.75 ± 18.25	14.88 ± 78.52	14.43 ± 91.02	9.03 ± 14.79	15.20 ± 17.21	16.16 ± 92.03	7.67 ± 10.35
	P	0.038	0.583	0.084	<0.001	<0.001	0.646	<0.001
1. M P V	No	10.01 ± 1.42	9.82 ± 1.31	9.93 ± 1.52	9.81 ± 1.44	10.02 ± 1.41	10.04 ± 1.54	10.03 ± 1.52
	Yes	10.02 ± 1.52	10.02 ± 1.51	10.03 ± 1.43	10.02 ± 1.44	9.81 ± 1.44	9.92 ± 1.32	9.93 ± 1.31
	P	0.668	0.061	0.281	0.048	0.017	0.209	0.408
2. M P V	No	10.29 ± 4.94	10.48 ± 7.50	9.93 ± 1.49	10.00 ± 1.62	10.29 ± 4.95	10.13 ± 1.42	10.22 ± 1.50
	Yes	10.09 ± 1.52	10.14 ± 1.51	10.53 ± 5.82	10.34 ± 5.05	10.10 ± 1.72	10.34 ± 5.88	10.27 ± 6.34
	P	0.948	0.149	0.219	0.802	0.665	0.183	0.037

(P, Mann-Whitney U test; DM, Diabetes Mellitus; HT-CRD, Hypertension-chronic kidney disease; CVD, Cardiovascular diseases; ND, Neurological diseases; PD, Lung Diseases.)

Table 4. Comparison of Hospitalization and Discharge Hematological Parameters According to the Survival Status of the Patients

Variables	All Patents (464)	Survived (317)	Died (147)	P**
1. WBC	10.48±5.94	10.20±5.69	11.06±6.44	0.258
2. WBC	10.87±6.77	9.26±5.31	14.34±8.16	<0.001
P*	0.948	0.003	<0.001	
1. Platelet	266.02±124.11	272.33±119.22	252.52±133.43	0.051
2. Platelet	259.11±134.43	277.01±129.34	220.53±137.41	<0.001
P*	0.139	0.414	0.002	
1. Neutrophil	8.16±5.13	7.74±4.52	9.07±6.18	0.035
2. Neutrophil	8.44±6.14	6.69±4.52	12.23±7.37	<0.001
P*	0.711	<0.001	<0.001	
1. lymphocyte	1.52±2.73	1.67±3.22	1.20±.99	<0.001
2. lymphocyte	1.54±1.43	1.56±.91	1.50±2.18	<0.001
P*	0.051	0.563	0.045	
1. PLR	255.71±196.42	235.13±156.61	300.08±257.60	0.017
2. PLR	246.29±217.26	229.56±185.16	282.37±271.22	0.476
P*	0.031	0.430	0.479	
1. NLR	8.90±10.82	7.52±8.13	11.88±14.67	<0.001
2. NLR	13.33±66.10	7.58±13.42	25.74±115.07	<0.001
P*	0.494	0.941	0.149	
1. MPV	10.01±1.43	9.92±1.41	10.14±1.53	0.288
2. MPV	10.24±4.28	10.10±5.03	10.54±1.78	<0.001
P*	0.168	0.536	<0.001	
1. PDW	15.14±2.32	15.02±2.23	15.13±2.41	0.188
2. PDW	15.47±7.64	14.99±2.27	16.52±13.13	<0.001
P*	0.299	0.724	0.194	
1. PCT	0.26±0.12	0.26±0.13	0.24±0.12	0.069
2. PCT	0.25±0.11	0.26±0.10	0.22±0.13	<0.001
P*	0.102	0.551	0.017	

(*:t-test; **: Mann-Whitney U test)

Discussion

Our study aimed to evaluate the thrombocyte indices, PLR and NLR values, mortality, and prognosis by examining the blood tests of the patients hospitalized in the palliative care service.

Malignancy and neurological diseases were more prominent as the primary diagnosis in patients in the palliative service. It is seen that 68.30% of the 464 patients were alive and 31.70% died during the study period. While the mortality was high in the presence of malignancy, it was lower in those with neurological disease. Since patients with malignancy have generally completed their treatment and are referred to the palliative care service in the terminal period, high mortality in these patients is a possible outcome.¹⁰ Patients with neurological diseases have problems such as nutritional problems, pressure ulcers, muscle tone disorder, and

infection, and therefore they need more care.¹¹ In a similar study conducted by Yuruyen et al.¹⁰, it was found that 52.1% of the patients in the palliative care service were discharged with recovery, 15.3% were referred, and 33.6% died. In our study, it was observed that the mortality (39.5%) of the patients in the palliative service transferred from the emergency room was numerically higher. This may be related to the fact that the patients taken over from the intensive care unit no longer need intensive care, and their general condition is relatively stable. It may also be related to the fact that the reasons for admission of patients referred from the emergency department are acute and serious problems.

Platelet indices obtained by complete blood count (MPW, PDW, PCT), PLR and NLR have recently been considered valuable in terms of their use as inflammatory markers.^{5,6} It attracts attention in terms of being affordable and easily accessible. At the same time, there are many studies that may be prognostic and mortality markers for various diseases.^{7,8} In our study, the patients had at least one chronic disease. NLR, PLR and exit NLR levels in the admission of patients with diabetes (27.61%) were found to be lower than those without diabetes. In a study by Sayiner et al.¹² in which they studied the relationship between NLR levels and microvascular complications of diabetes, NLR levels were found to be high in diabetic patients, and researchers attributed this increase to subclinical inflammation occurring in microvascular complications and reported that it is a cost-effective marker in demonstrating microvascular complications. Mertoglu et al.¹³ investigated whether NLR, PLR and MPV levels could be predictive markers in prediabetic and diabetic patients. The fact that the changes in NLR levels in diabetic patients in our study were different from other studies may be due to the presence of many other concomitant diseases and conditions in the patients at the same time.

It is argued that the physiological response of leukocytes in the systemic circulation to stress with the effect of granulocyte colony-stimulating factor, tumor necrosis factor-alpha, interleukin-1 and interleukin-6 in cancerous tissue causes an increase in neutrophil count and a decrease in lymphocytes.¹⁴ It has been suggested that changes in NLR and PLR may be associated with tumor growth and metastasis, and this may play a prognostic role. IL-6 is an important cytokine that stimulates tumorigenesis. There is a study showing a positive relationship between MPV and IL-6 and thrombopoietin.¹⁵ Özyalvaçlı et al., in their study on 120 patients with breast cancer and 50 patients with benign proliferative breast disease, reported that high preoperative NLR levels had a high predictive value in predicting malignant cases and NLR levels were a significant prognostic factor for breast cancer.¹⁶ In a study by Kulaksızoğlu et al. in which 492 colorectal cancer patients and 327 control groups were included, NLR and PLR values were found to be significantly higher than in the control group, and it was stated that high NLR and PLR levels in colorectal cancer patients could be an important biomarker in determining the disease.¹⁷ Similarly, there are studies showing that high PLR levels observed in malignancies such as ovarian, colorectal, esophageal, pancreatic, and endometrial cancer are associated with poor prognosis.¹⁹⁻²¹ In our study, 134 (28.91%) patients with malignancy had higher NLR and PLR levels and lower MPV levels at admission compared to patients without malignancy.

In our study, admission NLR, PLR values and discharge NLR values of patients with neurological diseases were found to be lower, and admission MPV levels were found to be higher than that of patients without neurological disease. In the study of Bolayır et al., it was reported that NLR and PLR levels increased in patients with acute-stage intracerebral hemorrhage and that this elevation was closely associated with short-term mortality in patients with intracerebral hemorrhage.²¹ In a study investigating whether NLR and MPV values can be used as predictive factors in stroke; While NLR levels were found to be higher in stroke patients than in healthy individuals, no association was found between MPV levels and stroke risk and stroke prognosis.²²

In our study, admission NLR, PLR and discharge NLR levels were lower, and discharge MPV levels were higher in patients with pressure ulcers compared to that of patients without. Pressure ulcers are more common in the intensive care unit, geriatric, and neurology services.²³ This explains why the comparison of NLR, PLR and MPV levels of patients with pressure ulcers had similar results with patients with neurological disorders in our study.

In our study, admission and discharge values of patients who died or survived were compared to investigate the effect of hematological parameters on mortality. Discharge WBC values of patients who died were found to be higher than the admission WBC values of patients who survived. In the patients who survived, discharge WBC values were found to be lower than admission WBC levels. Leukocytosis occurs in many conditions, especially in infection, inflammation, myeloproliferative diseases, and stress.²⁴ Akbas et al.²⁵ reported that leukocytosis has a predictive value in mortality. Thrombocytopenia is also an independent risk factor that increases mortality in critically ill patients.³ In the study of Coşkun et al., including 237 patients followed in the intensive care unit, thrombocytopenia was shown to be associated with high mortality.²⁶ In the study performed by Haksıyer et al. in the intensive care unit, the mortality rate was found to be higher in patients with thrombocytopenia, and it was reported that the most common causes of thrombocytopenia were sepsis and DIC.²⁷ In our study, discharge platelet levels of patients who died were lower than in admission values of the same patients and that of patients who survived. These results, similar to other studies, show that thrombocytopenia accompanies mortality.

Both neutrophilia and lymphopenia can be considered acute-phase reactants.⁴ In a study comparing patients with small cell lung cancer and the healthy group, increased neutrophil and decreased lymphocyte levels were associated with decreased survival.²⁸ In our study, when the neutrophil and lymphocyte values of the patients who died and the patients who survived were compared, it was observed that the neutrophil levels were high, and the lymphocyte levels were low, similar to the literature. When the admission and discharge blood values of the patients were compared, the discharge neutrophil value was found to be low in the patients who survived, while the discharge neutrophil and lymphocyte values were found to be high in the patients who died.

Many studies have shown a direct correlation between mortality and higher rates of NLR and PLR in different patient populations. Kutlucan et al.²⁹ showed that high PLR and NLR levels might be an indicator for the development of nosocomial infections and may prolong hospital stays. In our study, both admission and discharge NLR levels and admission PLR levels were found to be significantly higher in the patients who died compared to the patients who were alive.

Patients in critical care services, such as palliative care services and intensive care units, often have many different comorbidities. Therefore, it is very difficult to determine the effect of a particular disease on platelet indices (MPV, PDW, PCT) in palliative care services and intensive care units.³ In a study conducted to investigate the relationship between platelet indices and their performance in predicting disease severity and mortality, 261 critically ill patients were included; high MPV and PDW levels and low platelet and PCT levels have been associated with more severe disease and higher mortality compared to patients with normal platelet index.³⁰ Efe et al. investigated the prognostic importance of platelet indices in critically ill patients in the intensive care unit and found that MPV and PDW levels were correlated with each other.³ It has also been reported that they show a positive correlation with the severity of the disease and a negative correlation with the platelet count. In our study, discharge MPV and PDW levels were found to be higher in patients who died compared to patients who survived, while discharge PCT levels were found to be lower.³

The limitations of our study are that our study is a retrospective and single-center study and that our parameters are not compared as multiple measurements but just as two measurements, the first blood test after admission to the service and the last blood test before discharge from the service. The best aspect of our study is that it is the first original study to examine the platelet indices, NLR and PLR values of palliative care service patients. In addition, it is one of the few studies evaluating critically ill patients who are under the influence of many factors affecting hematological parameters. However, further multicenter, prospective and cohort studies are needed.

In this study, a contribution was made to the literature by evaluating platelet indices, platelet, neutrophil, lymphocyte values, NLR and PLR values, and prognosis and mortality in palliative care patients.

Conclusion

In our study, 31.70% of the patients hospitalized in the palliative service died. Mortality rates were found to be numerically higher in patients transferred from the emergency department with malignancy and lower in patients with neurological disease. In the last blood tests of the patients who died, leukocytosis, thrombocytopenia, lymphopenia, and neutrophilia were more common than the patients who survived. The admission NLR, PLR and discharge NLR, WBC, neutrophil, lymphocyte, MPV, and PDW levels were found to be higher in the patients who died, and the discharge platelet and PCT levels were found to be lower in the patients

who survived. It was observed that the mean of admission PLR value was higher than the discharge value. The discharge WBC and neutrophil values of the patients who survived were found to be lower than the admission values.

Ethical Considerations: The study was carried out with the approval of the E-77192459-050.99-3000 dated 14.01.2021 and numbered 2021/423 of the Non-Invasive Clinical Research Ethics Committee of the Faculty of Medicine of the local University.

Conflict of Interest: The authors declare no conflict of interest.

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