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COMPARISON OF COMPLETE BLOOD COUNTS OF STABLE COPD PATIENTS AT TWO DIFFERENT ALTITUDE IN TURKEY.

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ABSTRACT... Introduction: The aim of this study was to evaluate how altitude difference affects complete blood count (CBC) in patients with stable Chronic Obstructive Pulmonary Disease (COPD). **Study Design:** Cross-sectional study. **Setting:** Department of Pulmonology, Kars Harakani State Hospital (Group 1) and Samsun Chest Diseases and Thoracic Surgery Hospital (Group 2), Turkey. **Period:** Six months. From March to September 2018. **Material and Methods:** A total of 400 patients (200 female, 200 male) with stable COPD were included. For each group, 100 female and 100 male patients were randomly selected from hospitals. Age, BMI (kg/m^2), comorbidity, smoking status, CBC were evaluated. Hemoglobin, hematocrit, WBC, MPV, platelet, lymphocyte count and percentage, platelet/lymphocyte rate (PLR), neutrophil count and percentage, neutrophil /lymphocyte rate (NLR), eosinophil count and percentage, PDW, PCT were recorded. **Results:** Patients living at high altitude were significantly older, had lower weight and had lower FEV1 levels. COPD stages of Group 1 patients were more severe ($p<0.001$). There were no moderate COPD patients in this group and the patients had fewer comorbidities (43%). Hemoglobin, hematocrit, MPV, WBC, neutrophil count and percentage, NLR and PLR were significantly higher in Group 1 ($p<0.001$). PDW, PCT, lymphocyte count and percentage, eosinophil count and percentage were significantly higher in Group 2 patients ($p<0.001$). **Conclusion:** Hemoglobin, hematocrit, MPV, WBC, neutrophil count and percentage, NLR and PLR were higher in patients living at high altitude. PDW, PCT, lymphocyte count and percentage, eosinophil count and percentage were significantly higher in patients living at low altitude.

Key words: Altitude, Chronic Obstructive Pulmonary Disease, Complete Blood Count.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a global health problem and the third leading cause of mortality worldwide.[1,2] COPD is a common disease characterized by improperly reversible airflow limitation and alveolar abnormalities.[1,2] The most important risk factors for COPD are smoking, air pollution, age, tuberculosis exposure, socio-economic status and additionally geographical differences.[3] Around 400 million people live in high altitude (>1500 meters above sea-level) and this geographical altitude is associated with COPD prevalence, and adaptation mechanism of these patients.[4] In COPD patients living in high altitude areas, altitude could induce a higher growth of airways relative to lung size, causing to an increased FEV1/FVC ratio and it may cause chronic hypoxia.[5]

In high altitude, to compensate for the low pressure of oxygen, many physiological changes occur in the human blood circulation. In response to hypoxia, the humanbody adapts to the tissues by increasing the distribution of oxygen. Firstly, it is expected that the hemoglobin concentration of circulating hemoglobin concentration will increase from the complete blood count parameters.[6]

Studies on how altitude affects patients with healthy individuals and COPD are quite common. In this study, we focused on how altitude difference affects complete blood count parameters in patients with stable COPD.

METHODS

Study Design

This cross-sectional study was performed after

ethical committee approval with the parameters of 400 patients (200 female, 200 male) with known COPD and presented to Kars Harakani State Hospital, Kars, Turkey (called Group 1) and Samsun Chest Diseases and Thoracic Surgery Hospital, Samsun, Turkey (called Group 2) between March 2018 and September 2018. The parameters of the patients were obtained from the electronic data bank of the hospital. The study included the patients with known stable COPD who admitted to Chest Diseases Clinics of two different hospitals. For each group, 100 female and 100 male patients were randomly selected from both hospitals.

The evaluated parameters which belong to the patients are: age, height (meter), weight (kg), BMI (kg/m^2), COPD stages, comorbidity, smoking status (smoker, ex-smoker, never smoker). The results of complete blood cell count of the patients provided hemoglobin (g/dL), hematocrit (%), white blood cell (WBC, $\times 10^3 \mu$l), mean platelet volume (MPV, fL), platelet count ($\times 10^3 \mu$l), lymphocyte count ($\times 10^3 \mu$l), lymphocyte percentage (%), platelet/lymphocyte rate (division of platelet count in lymphocyte count, (PLR) neutrophil count ($\times 10^3 \mu$l), neutrophil percent (%), neutrophil /lymphocyte rate (division of neutrophil count in lymphocyte rate, NLR), eosinophil count ($\times 10^3 \mu$l), eosinophil percent (%), platelet distribution width (PDW, fL) plateletcrit (PCT, %). COPD was based on Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria for the diagnosis, classification and severity.[7] Spirometry was done with Spirolab III-MIR, Italy. Subsequently, patients were staged according to the severity criteria of GOLD.[7]; stage I (FEV1≥80%), stage II (50%≤FEV1<80%), stage III (30%≤FEV1<50 %) and stage IV (FEV1<30 %).[7]

Blood Samples

All blood samples were drawn from the vein in the forearm and collected into 2 mL Lavender (EDTA) top tube and were analysed with Pentra DF Nexus, Horiba Medical, Japan with Automated Cell Counter Methodology. The blood samples were stabilized optimally when run within in 4 hours of collection, stable for 24 hours at room temperature, and stable for 36 hours at 2 – 8 degrees C.

Altitude Differences

Kars, located in the northeast of Turkey, is a city which is 1768 meters above sea level.[8] In our country, Kars is one of the cities with the highest altitude.[9] Samsun, located in the north of Turkey, is a city which is 4 meters above sea level.[9] In our country, is one of the cities with the lowest altitude.[9]

Statistical Analysis

Parameters were analyzed with SPPS for Windows 23.0 version. The mean of the continuous variables in descriptive statistics was expressed with standard deviation; categorical variables were expressed with numbers and percentages. The significance of the difference between the groups was evaluated with Chi-Square Test. Mann-Whitney U Test was used in comparison of binary groups. Kruskal Wallis Test was used in comparison of groups more than two. $p<0.005$ value was accepted to be statistically significant.

RESULTS

Baseline characteristic features of patients are presented in Table-I. Patients living at high altitude were significantly older, had lower weight and had lower FEV1 levels. COPD stages of Group 1 patients were more severe ($p<0.001$). There were no moderate COPD patients in Group 1 and the patients had fewer comorbidities (43%). In Group 1, most of the patients were ex-smoker and never smoker (84.5%).

In Group 2, mild and moderate patient groups were higher (60%). In this group, the number of patients with additional diseases was higher (57.5%) and the number of smoker patients were higher than ex-smoker and never smoker (44.5%). Complete blood count parameters are presented in Table-II. Hemoglobin, hematocrit, MPV, WBC, neutrophil count, neutrophil percentage, NLR and PLR were significantly higher in Group 1 compared to Group 2 patients ($p<0.001$). PDW, PCT, lymphocyte, lymphocyte percentage, eosinophil and eosinophil percent were significantly higher in Group 2 compared to Group 1 patients ($p<0.001$).

	COPD Groups			P-Value
	Total	Group 1	Group 2	
	Mean±sd / n (%)			
Age	66.6±9.7	68.4±9.7	64.7±9.3	<0.001
Gender				
Female	200 (50%)	100 (50%)	100 (50%)	NS
Male	200 (50%)	100 (50%)	100 (50%)	
Length (meter)	1.6±0.1	1.6±0.1	1.6±0.1	NS
Weight (kg)	73±15.1	71.2±15.2	74.9±14.8	0.021
BMI (kg⁄m2)	27.9±5.9	27.4±6.1	28.4±5.7	NS
FEV1	47.3±19.9	39±15.2	55.6±20.6	<0.001
Group				
Mild ≥80%	32 (8%)	-	32 (16%)	<0.001
Moderate 50% ≤ FEV1 < 80%	142 (35.5%)	54 (27%)	88 (44%)	
Severe 30% ≤ FEV1 < 50%	135 (34.0%)	79 (39.5%)	57 (28.5%)	
Very Severe FEV1<30%	90 (22.5%)	67 (33.5%)	23 (11.5%)	
Comorbidity				
Exist	201 (50.3%)	86 (43%)	115 (57.5%)	0.004
Absent	199 (49.8%)	114 (57%)	85 (42.5%)	
Smoking Status				
Smoker	120 (30%)	31 (15.5%)	89 (44.5%)	<0.001
Ex-Smoker	151 (37.8%)	86 (43%)	65 (32.5%)	
Never Smoker	129 (32.3%)	83 (41.5%)	46 (23%)	

COPD, chronic obstructive pulmonary disease; continuous variables are expressed as mean ± standard deviation; NS, non-significant; BMI, body mass index; FEV1, forced expiratory volume in one second.

Table-I. Baseline characteristics features of Group 1 and Group 2 patients

	COPD Groups			P-Value
	Total	Group 1	Group 2	
	Mean±sd / n(%)			
Hemoglobin	14.14±2.91	15.18±2.06	13.09±3.26	<0.001
Hematocrit	42.6±11	46.3±6.5	38.8±13	<0.001
MPV	7.86±1.24	8.21±0.97	7.51±1.37	<0.001
Platelet count (x10^3)	258.2±82	255.1±79.3	261.3±84.6	NS
PDW	17.9±15	16.8±0.7	18.9±21.1	<0.001
PCT	0.69±9.91	0.2±0.06	1.19±14.05	0.021
WBC (x10^3)	10.46±6.07	11.24±4.69	9.66±7.12	<0.001
Lymphocyte count	1.96±1.45	1.55±0.94	2.37±1.73	<0.001
Lymphocyte (%)	20.9±12	15.9±11	25.9±10.9	<0.001
Neutrophil count	7.6±4.97	8.68±4.57	6.52±5.12	<0.001
Neutrophil (%)	71.4±26.7	77.5±34.8	65.3±12.2	<0.001
Eosinophil count	0.17±0.28	0.16±0.31	0.19±0.26	<0.001
Eosinophil (%)	1.9±2.7	1.5±2.5	2.2±2.8	<0.001
NLR	6.38±9.76	8.91±12.37	3.86±5.02	<0.001
PLR	184.6±182	230.5±231.7	138.6±92.2	<0.001

COPD, chronic obstructive pulmonary disease; continuous variables are expressed as mean ± standard deviation; NS, non-significant; MPV, mean platelet volume; PDW, platelet distribution width; PCT, plateletcrit; WBC, white blood cell; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

Table-II. Complete blood count parameters of Group 1 and Group 2 patients

DISCUSSION

Our results demonstrate that patients living at high altitude were significantly older, had lower weight and had lower FEV1 levels. COPD stages of these patients were more severe. None of the patients in this group had mild COPD. Moreover, the patients in this group had fewer comorbidities and most of the patients were ex-smoker and never smoker. Patients living at low altitude, mild and moderate COPD stages were higher. In addition, the number of patients with comorbidities and smoking were higher. In patients with low altitude, smoking and comorbidities are high, however, moderate COPD levels in these patients may be attributed to age and less exposure to hypoxia. COPD is a disease with increasing prevalence and severity with age.[10] Cumulative exposure to smoking and pollution, telomere shortening and dysfunction, decreased vital capacity in the aging lung, reduced recoil, mucociliary clearance, mucosal immunity and decreased vascular reserve may increase the severity of the disease with age.[10] It is known that deterioration of gas exchange will be impaired by exposure to hypoxic environment in patients with COPD.[11]

In this study, hemoglobin, hematocrit, MPV, WBC, neutrophil count, neutrophil percentage, NLR and PLR were higher in patients living at high altitude. Increased hemoglobin and hematocrit in patients living at high altitude is an expected adaptation to more oxygen uptake in tissues. In these patients, higher MPV indicates increased platelet function and aggregation. Although these patients are stable, the number of neutrophils and the high percentage may be due to their severity of disease and frequent use of steroids. In the study of Al-Sweedan et al., hemoglobin, MPV and leukocyte counts were significantly higher in patients living at high altitude.[12] Stress hormones secreted at high altitude may also increase neutrophil count and decrease lymphocyte count.[13] Increased neutrophil counts and decreased lymphocyte counts cause NLR and TLR to increase in this group of patients.

PDW, PCT, lymphocyte, lymphocyte percentage, eosinophil and eosinophil percentage were significantly higher in patients living at low altitude. PDW is one of the markers of platelet activation. High PDW is an indicator of inflammatory process and hypercoagulability.[14] PDW is expected to be higher in COPD patients compared to healthy people.[14] There are studies showing that PDW is correlated with increasing age and MPV.[15] In our study, there is a reverse finding for PDW. Smoking may disrupt the morphology of platelets and cause PDW to be high in this group. PCT is a measure of total platelet mass and MPV is the average size of platelets. PCT and MPV are parameters that can be affected by comorbid conditions in age group patients like our study.[16] PCT was expected to increase in patients with severe COPD, but in our study, it was low.[17] In the study of Zhang et al., PCT was negatively correlated with age, but not with low altitude.[15] The number and percentage of lymphocytes were lower in Group 1. Lymphocyte is the expected parameter to decrease in older age and more advanced lung disease. Low lymphocyte count is a physiological adaptation mechanism of the immune system to increasing age.[18] Additively, lymphocyte count is expected to decrease at high altitude.[19] Eosinophilia in patients living at low altitude may be attributed to better response to steroid treatment and greater number in the early stage. The high rate of smoking in this group may cause eosinophilia.[20,21,22]

The inclusion of only two centers in the study, the low number of patients and the high number of patients with severe COPD in Group 1 are the limitations of the study.

CONCLUSION

In conclusion, hemoglobin, hematocrit, MPV, WBC, neutrophil count, neutrophil percentage, NLR and PLR were higher in patients living at high altitude. PDW, PCT, lymphocyte, lymphocyte percentage, eosinophil and eosinophil percent were significantly higher in patients living at low altitude.

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