DOI: 10.37990/medr.1479602 Med Records 2024;6(3):354-9

MEDICAL RECORDS-International Medical Journal

Research Article

# An Investigation of the Effect of Anemia on Prognosis in Chronic Obstructive Pulmonary Disease

Zuhal Ozer Simsek, Inci Gulmez

Erciyes University, Faculty of Medicine, Department of Chest Diseases, Kayseri, Türkiye



**Abstract**

**Aim:** The majority of healthcare facility admissions in individuals with chronic obstructive pulmonary disease (COPD) are attributable to exacerbations, known to negatively impact prognosis. This study aims to examine the relationship between anemia in COPD patients and the frequency of exacerbations, and consequently, its effect on prognosis.

**Material and Method:** Twenty-nine anemic, 30 normocytic, and 28 polycythemic patients diagnosed with COPD were enrolled and evaluated based on their Forced Expiratory Volume in One Second (FEV1) values, symptoms, exercise ability, and number of exacerbations. At one-year follow-up appointments, the history of emergency department visits, outpatient clinic visits, intensive care admissions, and hospitalizations requiring respiratory support during the year were recorded for patients.

**Results:** Similar to other research on anemia in COPD, the anemia seen in the current study was most typically consistent with chronic disease anemia. When the anemic group was compared with the normostemic and polycystic groups with regard to the frequency of exacerbations, both the count of emergency department visits and hospitalizations requiring intensive care were found to be statistically meaningfully higher in the anemic group compared to the non-anemics.

**Conclusion:** The results obtained in the present study show that anemia in COPD is associated with increased hospital admissions and exacerbations. Given that increased exacerbation frequency is a known poor prognostic factor, it can be inferred that anemia, by increasing exacerbation frequency, contributes to poor prognosis.

**Keywords:** Chronic obstructive pulmonary disease, anemia, exacerbation, prognosis

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is defined as persistent and often progressive airflow restriction accompanied by chronic respiratory symptoms (1). It ranks third among the leading causes of death worldwide (2). COPD develops as a result of a chronic inflammatory process triggered primarily by harmful gases and particles, notably cigarette smoke. Inflammation not only remains confined to the lungs but also exhibits systemic characteristics (3). In COPD, compensatory secondary erythrocytosis is expected to occur to correct tissue oxygen transport impaired by prolonged hypoxemia (4). However, contrary to popular belief, polycythemia is observed in approximately 6% of COPD patients, while anemia is a much more common finding, occurring in 13-33% of patients (5). Anemia develops in COPD patients due to a variety of factors, including nutritional deficiencies, stress ulcers particularly in the context of frequent systemic steroid use, continued smoking leading to carboxyhemoglobinemia and shortened mean erythrocyte lifespan due to chronic inflammation, erythropoietin resistance, and disruption of iron homeostasis (6). It is known that in COPD, chronic inflammation causes a decrease in the proliferative response to erythropoietin and a shortening of the lifespan of red blood cells. In addition, in COPD, anemia of chronic disease develops due to factors such as a decrease in erythropoietin production triggered by hypoxia, deterioration in iron metabolism, and iron deficiency due to malnutrition (7,8). Anemia in COPD

CITATION

Simsek Z, Gulmez I. An Investigation of the Effect of Anemia on Prognosis in Chronic Obstructive Pulmonary Disease. Med Records. 2024;6(3):354-9. DOI:1037990/medr.1479602

**Received:** 08.05.2024 **Accepted:** 24.07.2024 **Published:** 29.08.2024

**Corresponding Author:** Zuhal Ozer Simsek, Erciyes University, Faculty of Medicine, Department of Chest Diseases, Kayseri, Türkiye

**E-mail**: drzosimsek@gmail.com

is associated with impaired tissue oxygen transport, exercise intolerance, and increased mortality. Studies have shown that in COPD, characteristics of anemia are highly consistent with chronic disease anemia (CDA) (9,10). CDA is a form of anemia that can arise in various conditions, both immune and non-immune, such as infection, inflammation, neoplastic diseases, severe trauma, heart failure, and diabetes mellitus (11). In a two-year prospective study involving 130 patients aimed at determining the frequency of anemia in COPD, it was found to be 6.2%. Additionally, in the anemic group, statistically significantly lower body mass index (BMI), higher erythropoietin, and interleukin-6 (IL-6) assays were found compared to non-anemic individuals (12). Anemic COPD patients have a greater mortality rate and require longer hospitalizations than non-anemic individuals (13). It is known that increased hospital admissions due to acute exacerbations result in a worse patient prognosis (14). There are few studies about the effects the effects of anemia on exacerbation frequency and, consequently, prognosis. The purpose of this study was to examine the effect of anemia on exacerbation frequency and, consequently, the prognosis of COPD.

## MATERIAL AND METHOD

Following local ethics committee approval on November 18. This study is a prospective observational study. Ethics permission was obtained before starting the study (project number: 2394). Twenty-nine anemic, 30 normocytic, and 28 polycythemic patients diagnosed with COPD were enrolled in the study. Patients with chronic kidney failure, chronic liver failure, acute and chronic infections, autoimmune diseases, malignancies, a history of heart failure, hematological diseases, and gastrointestinal bleeding, which can be causes of anemia, were excluded from the study. Three patients with malignancies detected during follow-up were excluded. As a total, 87 individuals included in the study were observed for one year. Tests for chronic disease anemia, iron deficiency anemia, vitamin B12, and folate deficiency were requested. The threshold value for anemia was accepted as a hemoglobin concentration of <13 g/dL for males and 12 g/dL for females (15).

The diagnostic criteria for chronic disease anemia include hemoglobin concentration under 13 g/dL in males and 12 g/dL in females, absence of another cause to explain anemia, normal or elevated serum ferritin levels, low total iron-binding capacity and transferrin saturation, and normal levels of vitamin B12 and folate (16).

All patients diagnosed with COPD were evaluated based on their Forced Expiratory Volume in One Second (FEV1) values, symptoms, exercise ability, and exacerbation frequency. The modified Medical Research Council (mMRC) dyspnea classification was administered for the evaluation of symptoms (17). The patients' physical activity ability was evaluated using the 6-minute walking distance (6MWD) test.

The BODE index (body mass index [BMI], airflow obstruction, dyspnea, and exercise capacity in COPD) was appraised (Table 1). This index is calculated based on four predictors. Body mass index (BMI), FEV1, mMRC dyspnea scale, and the 6MWD test. Scoring is done in four ways in the BODE index. The highest score is indicative of the worst disease.

At one-year follow-up appointments, the history of emergency department visits, outpatient clinic visits, intensive care admissions, and hospitalizations requiring respiratory support during the year were questioned through face-to-face interviews or telehealth consultations.

**Table 1. BODE index calculation**

| Variables | 0 | 1 | 2 | 3 |
|---|---|---|---|---|
| FEV1 (% of predicted) | >65 | 50-65 | 35-49 | <35 |
| mMRC Dyspnea Scale | 0-1 | 2 | 3 | 4 |
| 6MWD (meters) | >350 | 250-349 | 150-249 | <149 |
| BMI (kg/m²) | >21 | <21 | - | - |

FEV1: forced expiratory volume in one second, mMRC: modified medical research council, 6MWD: 6-min walking distance, BMI: body mass index

### Statistical Analysis

Statistical assessments were carried out using the SPSS (Statistical Package for Social Sciences) 15.0 software (Chicago, IL). Quantitative variables were pointed out as mean and standard deviation values, while qualitative variables were expressed as numbers and percentages. Parameters were compared for normal distributions using the Student's t-test and for non-normal distributions using the Mann-Whitney U test. Qualitative variables were assessed using the Chi-Square test. The mean values of quantitative variables before and after treatment in each group were assessed by the Paired-Samples T-test. A p value of <0.05 was defined as statistically significant in all analyses.

## RESULTS

A total of 87 patients with COPD (29 anemic, 30 normocytic, 28 polycythemic) were included in this research.

The demographic features of the patients are shown in Table 2.

**Table 2. Demographics and characteristics of the patients**

| | Anemic | Normocytic | Polycythemic |
|---|---|---|---|
| **Male (n)** | 24 | 26 | 24 |
| **Female (n)** | 5 | 4 | 4 |
| **Smoking (pack-years)** | 43.5±4.8 | 36.9±4.8 | 46.9±6.7 |
| **Never smoked** | 5 | 2 | 4 |
| **Ex-smoker** | 23 | 21 | 21 |
| **Current smoker** | 1 | 7 | 3 |
| **LTOT +** | 10 | 24 | 12 |
| **LTOT -** | 19 | 6 | 14 |
| **No comorbidities** | 15 | 13 | 14 |
| **Exitus** | 1 | 0 | 2 |
| **6MWD** | 0 (0-420) | 400 (0-550) | 330 (0-580) |
| **Annual number of emergency-outpatient clinic visits** | 5 (0-20) | 0 (0-20) | 1 (0-15) |
| **Annual number of intensive care hospitalizations** | 1 (0-3) | 0 (0-2) | 0 (0-2) |
| **Ferritin (14-30 ng/ml)** | 157.0±29.2 | | |
| **Folic acid (4.6-18.7 ng/mL)** | 9.7±0.9 | | |
| **Vitamin B12 (214-900 pg/mL)** | 530.8±69.8 | | |

Parametric data is shown as mean±S.E.M or median (minimum-maximum); 6MWD: 6-min walking distance, LTOT: long-term oxygen therapy

When comparing anemic and normocytic patients (Table 3), the anemic group was older (p=0.03), had a lower FEV1 value (p=0.02), and had a statistically meaningful shorter 6MWD (p<0.05). BMI and smoking (pack-years) showed no significant differences.

When comparing anemic and polycythemic patients (Table 3), the two groups had no significant age differences, FEV1 value, and smoking history. However, when compared based on BMI, the anemic group had a lower BMI (p=0.02), and the 6MWD was meaningfully shorter in the anemic patients (p<0.001).

BMI was highest in the polystemic group and lowest in the anemic group. This result was statistically meaningful (p=0.03).

**Table 3. Comparison of laboratory, demographic and respiratory parameters of the patients**

| | Anemic | Normocythemic | Polycythemic | P1 | P2 |
|---|---|---|---|---|---|
| **Age (years)** | 67.1±1.6 | 60.5±2.5 | 63.0±1.8 | 0.03 | 0.10 |
| **BMI (kg/m²)** | 25.7±0.8 | 26.3±0.7 | 29.2±1.3 | 0.59 | 0.02 |
| **Hemoglobin (g/dl)** | 11.7±0.1 | 14.6±0.1 | 17.8±0.2 | <0.001 | <0.001 |
| **Hematocrit (%)** | 37.0±.5 | 44.1±0.5 | 55.3±0.7 | <0.001 | <0.001 |
| **FEV1 (%)** | 45.1±4.1 | 59.6±4.1 | 47.7±3.5 | 0.02 | 0.64 |
| **FEV1 (ml)** | 112.7±10.1 | 175.9±11.4 | 126.9±10.3 | 0.03 | 0.05 |
| **6MWD (m)** | 93.4±25.6 | 388.0±23.3 | 286.4±32.4 | <0.001 | <0.001 |

P1: anemic-normocytic P2: anemic-polycythemic comparison; parametric data is expressed as mean±S.E.M or median (minimum-maximum); BMI: body mass index, 6MWD: 6-min walking distance, FEV1: forced expiratory volume in one second

When mMRC dyspnea score and BODE score were compared between the anemic and non-anemic groups (Table 4), both scores were higher in the anemic group. This result was statistically significant (p<0.001).

When comparing the mean hemoglobin levels of 39 patients receiving Long-Term Oxygen Therapy (LTOT) and 48 patients not receiving LTOT, no significant difference was found (14.9±0.3 and 14.3±0.5, respectively, p=0.35).

**Table 4. Comparison of mMRC and BODE scores between anemic and non-anemic subjects**

| | Anemic (n: 29) | Non-anemic (n: 58) | p |
|---|---|---|---|
| **mMRC** | 3 (0-4) | 2 (0-4) | <0.001 |
| **BODE** | 7 (0-10) | 3 (0-10) | <0.001 |

Parametric data is shown as median (minimum-maximum); mMRC: modified medical research council, BODE: body mass index, airflow obstruction, dyspnea, and exercise capacity in COPD

When comparing exacerbation frequency among the anemic, normocytic, and polycythemic groups, it was found that both emergency department and outpatient clinic visits, as well as the number of hospitalizations requiring intensive care, were higher in the anemic group (Table 5). This difference was statistically significant (p<0.01).

**Table 5. Comparison of patients in terms of exacerbation frequency**

| | | Average number of visits | P |
|---|---|---|---|
| **Annual emergency - outpatient clinic visits** | **Anemic** | **6.6±0.9** | <0.001 |
| | **Normocytic** | **1.8±0.7** | |
| **Hospitalization requiring intensive care** | **Anemic** | **0.8±0.1** | <0.001 |
| | **Normocytic** | **0.1±0.0** | |
| **Annual emergency - outpatient clinic visits** | **Anemic** | **6.6±0.9** | 0.01 |
| | **Polycythemic** | **3.4±0.9** | |
| **Hospitalization requiring intensive care** | **Anemic** | **0.8±0.1** | < 0.001 |
| | **Polycythemic** | **0.2±0.1** | |

Parametric data is expressed as mean ±S.E.M

During the one-year follow-up, two polycythemic patients and one anemic patient died. In the normostemic group, all patients were alive after one year. Statistical evaluation of patient groups in terms of mortality could not be performed due to a total of 3 patient deaths.

When anemic COPD patients were evaluated for the etiology of anemia, 21 patients (72.5%) were consistent with chronic disease anemia.

## DISCUSSION

An increasing body of evidence has shown that COPD is a more complex disease than a simple airway restriction. Factors associated with mortality in COPD include malnutrition, increased dyspnea, decreased exercise capacity, and the presence of comorbid conditions (18).

In assessing the severity of COPD and mortality risk, multidimensional indices like BODE are commonly used, but FEV1 alone can also be utilized (19). Higher BODE score were related with a higher mortality (20).

Although polycythemia is commonly assumed to be the most prevalent hematologic abnormality in COPD, studies have demonstrated that anemia is actually more commonly observed (9). In a prospective study by C. Cote et al. involving 683 stable COPD patients, the prevalence of anemia was found to be 17%, while the prevalence of polycythemia was 6%. In contrast, there are also publications stating that the percentage of anemia is lower in COPD (9,12). It is difficult to define the true percentage of anemia in COPD. Factors such as the omission of patients' comorbidities, inclusion of different patient groups, variations in the severity of lung disease, differences in age distribution, and socioeconomic disparities can affect the true prevalence of anemia etiologies. Previous studies revealed that the percentage of anemia in COPD ranges from 7.5% to 34% (21).

It was also shown that hematocrit value decreases with age and increasing severity of obstruction in COPD, while it increases with increasing BMI (22). In one study, it was reported that anemia can be observed in up to 10% of people over the age of 65. In the same study, nutritional factors -especially iron deficiency-, chronic inflammation, and unexplained causes were suggested to be the most common causes in the occurrence of senile anemia (23). In this study, when comparing the anemic and normocytic groups, it was observed that anemic patients were older and had lower FEV1 values, while their BMI values were similar. While anemia and polycythemia patients showed no difference in terms of age and FEV1, BMI was found to be lower in anemic patients. However, the mean BMI of the anemic group was still within the normal range. Considering that anemic patients included in the present study were older, Senility may be an influential factor in the developming of anemia in these patients.

One important factor associated with mortality in COPD is the post-bronchodilator FEV1 value. There are publications showing that the BODE index is superior to FEV1 alone in determining mortality in COPD (19). In the present study, mean BODE score was 10 in anemic patients and 6 in polycythemic patients. It was observed that as FEV1 values decreased, the frequency of anemia increased, hospital admissions were more frequent, and although statistical evaluation could not be performed, mortality appeared to be higher in anemic patients compared to non-anemic ones.

Boutou AK et al. investigated the prevalence of anemia in COPD and its impact on exercise and dyspnea. Anemic patients were found to be older, had lower FEV1 values, and had higher mMRC dyspnea scores, indicating more severe disease (24). In this investigation, there was no distinction between anemic and non-anemic patients in terms of BMI, smoking, and LTOT. When comparing the anemic and normocytic groups, similar results were found. However, when the anemic and polycythemic groups were compared, there were no notable differences in age, FEV1 values, or smoking history, but anemic patients had a significantly lower BMI. In Cote et al.'s study, the anemic group also had significantly higher mMRC dyspnea scores

and shorter 6MWD (9). A decrease in 6MWD was found to be associated with a decrease in survival. Anemia has been found to be a crucial factor in decreased exercise capacity and increased dyspnea. In the present study, between the anemic group and the non-anemic group, significantly higher mMRC and BODE scores, as well as shorter 6MWD results, were obtained. The mMRC dyspnea score has been shown to be a predictor of expected survival (25). The 6MWD is a test that has been recognized as a determinant for functional status and mortality (26). In the present study, it was shown that the 6MWD was lower in anemic patients compared to non-anemic ones. When looking at the three patients with mortality, consistent with the literature, all three patients had high mMRC dyspnea scores and the 6MWD was less than 250 meters.

In the study by Cote et al., the median survival of COPD patients was 49 months in the anemic group and 74 months in the non-anemic group. In another investigation by Halpern et al., it was observed that the mortality rate in the anemic COPD group was twice as high as in the non-anemic COPD group (27). The most extensive research of increased mortality related to low hemoglobin levels in COPD is the ANTADIR (Association Nationale pour le Traitement à Domicile de l'Insuffisance Respiratoire) study. In a 10-year retrospective analysis of 2524 patients with COPD, the percentage of anemia was discovered to be 12.6% in males and 8.2% in females. 3-year survival rate was 24% among those with a hematocrit value below 35% compared to 70% among those with a hematocrit value above 55% (28). In the present study, one anemic patient and two polycythemic patients died during one year of observation. In the normocytic group, all patients were alive at the end of the year. Statistical evaluation could not be made because of the low number of deaths, but these results suggested that the prognosis was better in the normocytic group. The impact of average hemoglobin levels on mortality could have been more clearly evaluated if the follow-up period of patients had been longer than one year. This was one of the limitations of the study.

In the current investigation, no difference was identified in hemoglobin levels with respect to LTOT use. The shorter 6MWD in patients using LTOT can be explained by the fact that these were more severe cases due to lower FEV1 values.

Exacerbations of COPD are defined as acute deteriorations characterized by changes in the patient's daily respiratory symptoms and necessitating alterations in current treatment (29). Exacerbations are responsible for a significant portion of health care and are known to negatively impact quality of life and prognosis (30). Low hematocrit levels are associated with increased hospital admission frequency and length of stay, leading to increased morbidity and mortality (28). Differently, in a recent study, patients who were hospitalized due to COPD exacerbations were followed for 3 months after discharge. There was no significant difference in attack frequency in anemic patients, but mortality was observed to be higher (31). In the present study, between the anemic group and the non-anemic group in terms of exacerbation frequency, significant differences were observed in both emergency and outpatient visits and the number of hospital admissions requiring intensive care. Consistent with the literature, these findings show that anemia is a poor prognostic factor for COPD.

The main limitations of the investigation are the small number of patients, the short observation period, and the inability to follow the variability in anemia parameters during the follow-up period.

## CONCLUSION

In conclusion, anemia in COPD is a poor prognostic factor associated with increased hospital admissions and exacerbation frequency, reduced functional capacity, and worsened dyspnea. It should be considered that anemic patients with COPD are more severe cases. Although the impact on mortality was not directly evaluated in this study, the outcomes indirectly infer that an increased frequency of exacerbations may lead to an increase in mortality.

***Financial disclosures:*** *The authors declared that this study has received no financial support.*

***Conflict of interest:*** *The authors have no conflicts of interest to declare.*

***Ethical approval:*** *Approval was obtained from the local Ethics Committee of Erciyes University Faculty of Medicine with the decision number 09/166 dated 07.04.2009.*

## REFERENCES

1. Celli B, Fabbri L, Criner G, et al. Definition and Nomenclature of Chronic Obstructive Pulmonary Disease: Time for Its Revision. Am J Respir Crit Care Med. 2022;206:1317-25.
2. WHO. Chronic obstructive pulmonary disease (COPD). https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd) access date 15.03.2022
3. Guo P, Li R, Piao TH, et al. Pathological mechanism and targeted drugs of COPD. Int J Chron Obstruct Pulmon Dis. 2022;17:1565-75.
4. Pillai AA, Fazal S, Mukkamalla SKR, Babiker HM. Polycythemia. 2023 May 20. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan.
5. Similowski T, Agustí A, MacNee W, Schönhofer B. The potential impact of anaemia of chronic disease in COPD. Eur Respir J. 2006;27:390-6. Erratum in: Eur Respir J. 2006 May;27(5):1076.
6. Weiss G, Goodnough LT. Anemia of chronic disease. N Engl J Med. 2005;352:1011-23.
7. Xiang Y, Luo X. Extrapulmonary comorbidities associated with chronic obstructive pulmonary disease: a review. Int J Chron Obstruct Pulmon Dis. 2024;19:567-78.
8. Inoue S. Anemia and iron deficiency in chronic obstructive pulmonary disease. Respir Investig. 2023;61:485-6.

9. Cote C, Zilberberg MD, Mody SH, et al. Haemoglobin level and its clinical impact in a cohort of patients with COPD. Eur Respir J. 2007;29:923-9.
10. John M, Hoernig S, Doehner W, et al. Anemia and inflammation in COPD. Chest. 2005;127:825-9.
11. Weiss G. Pathogenesis and treatment of anaemia of chronic disease. Blood Rev. 2002;16:87-96.
12. Comeche Casanova L, Echave-Sustaeta JM, García Luján R, et al. Prevalence of anaemia associated with chronic obstructive pulmonary disease. Study of associated variables. Arch Bronconeumol. 2013;49:383-7.
13. Vijayan VK. Chronic obstructive pulmonary disease. Indian J Med Res. 2013;137:251-69.
14. Harries TH, Thornton HV, Crichton S, et al. Length of stay of COPD hospital admissions between 2006 and 2010: a retrospective longitudinal study. Int J Chron Obstruct Pulmon Dis. 2015;10:603-11.
15. World Health Organization . Iron deficiency anemia. assessment, prevention, and control. A guide for programme managers. Geneva: WHO; 2001;34-5.
16. Madu AJ, Ughasoro MD. Anaemia of chronic disease: an in-depth review. Med Princ Pract. 2017;26:1-9.
17. Bestall JC, Paul EA, Garrod R, et al. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. Thorax. 1999;54:581-6.
18. Almagro P, Calbo E, Ochoa de Echagüen A, et al. Mortality after hospitalization for COPD. Chest. 2002;121:1441-8.
19. Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. N Engl J Med. 2004;350:1005-12.
20. Ong KC, Earnest A, Lu SJ. A multidimensional grading system (BODE index) as predictor of hospitalization for COPD. Chest. 2005;128:3810-6.
21. Yohannes AM, Ershler WB. Anemia in COPD: a systematic review of the prevalence, quality of life, and mortality. Respir Care. 2011;56:644-52.
22. Bolton CE, Ionescu AA, Shiels KM, et al. Associated loss of fat-free mass and bone mineral density in chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2004;170:1286-93.
23. Guralnik JM, Eisenstaedt RS, Ferrucci L, et al. Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. Blood. 2004;104:2263-8.
24. Boutou AK, Stanopoulos I, Pitsiou GG, et al. Anemia of chronic disease in chronic obstructive pulmonary disease: a case-control study of cardiopulmonary exercise responses. Respiration. 2011;82:237-45.
25. Nishimura K, Izumi T, Tsukino M, Oga T. Dyspnea is a better predictor of 5-year survival than airway obstruction in patients with COPD. Chest. 2002;121:1434-40.
26. Pinto-Plata VM, Cote C, Cabral H, et al. The 6-min walk distance: change over time and value as a predictor of survival in severe COPD. Eur Respir J. 2004;23:28-33.
27. Halpern MT, Zilberberg MD, Schmier JK, et al. Anemia, costs and mortality in chronic obstructive pulmonary disease. Cost Eff Resour Alloc. 2006;4:17.
28. Chambellan A, Chailleux E, Similowski T; ANTADIR Observatory Group. Prognostic value of the hematocrit in patients with severe COPD receiving long-term oxygen therapy. Chest. 2005;128:1201-8. Erratum in: Chest. 2006;129:831.
29. Global Initiative for Chronic Obstructive Lung Disease Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (2020 report). https://goldcopd.org/wp-content/uploads/2019/11/GOLD-2020-REPORT-ver1.0wms.pdf access date 06.12.2019
30. Spencer S, Calverley PM, Burge PS, Jones PW. Impact of preventing exacerbations on deterioration of health status in COPD. Eur Respir J. 2004;23:698-702.
31. Rimal S, Das SK, Basnet A, et al. Prevalence and clinical impact of anemia in patients diagnosed with chronic obstructive pulmonary disease: a cross-sectional study. Health Sci Rep. 2023;6:e1371.