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# Relationship between lipid profile and monocyte to highdensity lipoprotein ratio with disease severity in chronic obstructive pulmonary disease patients

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## ABSTRACT

**Aim:** To examine lipid profile and monocyte to high density lipoprotein ratio ratio (MHR) values in stable chronic obstructive pulmonary disease patients.

**Material and Method**: Patients admitted to our hospital with the diagnosis of chronic obstructive pulmonary disease (COPD) between 01.01.2014 - 01.01.2020 were included in the study and evaluated retrospectively. According to the COPD guideline, two main groups were formed as A+B and C+D. Demographic characteristics, hemogram, C-Reaktif protein (CRP), albumin, lipid profile values were analyzed.

**Result:** In our study, there were 360 cases, 293 (81.4%) of which were male. The mean age was 67.61±8.7 years. There were 162 cases (45%) in the A+B group and 198 (55%) in the C+D group.White blood cell (WBC) , neutrophil, lymphocyte, neutrophil/ lymphocyte ratio (NLR), monocytes, hemoglobin, CRP, Albumin, high density lipoprotein (HDL), monocyte to HDL ratio (MHR) were found to be different at the level of statistical significance, while cholesterol, triglyceride and low density lipoprotein (LDL) were not at this level of significance. When evaluated with multivariate regression analysis afterwards, it was observed that the statistical significance levels of MHR, CRP and albumin values continued.

**Conclusion:** We think that high MHR rate, high CRP, and low albumin values in stable COPD patients may be a stimulant for increased disease severity.

**Keywords:** Albumin, CRP, COPD, HDL, lipit profile, MHR

## INTRODUCTION

COPD is an important chronic disease, the most important cause of which is tobacco use, with significant morbidity and the 3rd most frequent mortality results all over the world. According to the global iniative for chronic obstructive lung disease (GOLD) 2021 guideline, it is divided into A, B, C, D groups from mild to severe clinical according to the Unified COPD assessment determined according to symptoms and exacerbation history (1). The lower the fev1 value, which is the respiratory function parameter, is detected in COPD patients, the higher the mMRC and CAT values, which are symptom indicators. There is a negative correlation between low FEV1 values and group C and D with advanced COPD. This means that FEV1 values are expected to be significantly lower in groups C and D. When evaluated according to the GOLD 2021 guideline, the more advanced the COPD, the higher the morbidity and mortality is expected according to the combined COPD assessment consisting of symptoms and exacerbations (1,2). COPD is a systemic inflammatory disease and may be associated with many diseases, especially cardiovascular diseases (1).

In case of persistence of inflammation in COPD, other organs may also be damaged and related diseases may occur (3,4). The incidence of comorbid metabolic syndrome and low HDL in COPD is higher than in normal healthy individuals (5). There are studies showing that HDL has antiatherogenic, antioxidant and anti-inflammatory properties (6,7). Other lipid abnormalities that tend to accompany low HDL include elevated triglyceride levels, especially in the presence of a high ratio of LDL-C to HDL (6).

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Monocytes are a cell type that increases the inflammatory process and may be associated with increased oxidative stress (8,9). Considering the relationship of both monocytes and HDL with inflammation, there are studies showing that the MHR ratio may be an indicator of systemic inflammation (10,11)

There are limited studies in the literature examining the relationship between COPD lipid profile and there are conflicting results in the relationship between monocyte/HDL ratio, HDL and other lipids, airway restriction and disease severity in COPD (11-16).

For this purpose, our primary aim in our study is to separate the COPD groups as A+B and C+D groups and to analyze the lipid profile and MHR data in terms of their relationship with disease severity and their ability to be a biomarker. Additionally, to examine demographic data, clinical characteristics and other laboratory data.

## MATERIAL AND METHOD

Patients who applied to our hospital with the diagnosis of COPD between 01.01.2014-01.01.2020 were included in the study. This study was approved by the Health Sciences University Keçiören Education and Training Hospital Clinical Studies Ethics Board (Date: 22.03.2022, Decision No: 2012-KAEK-15/2490). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The study group consisted of the patients who met the lipid panel and inclusion criteria as soon as the patients were evaluated in their stable periods. Patients were defined according to the combined COPD assessment classification according to the 2022 GOLD guideline; Two main groups were formed as A+B and C+D groups. Demographic and clinical characteristics and laboratory characteristics were analyzed. In addition, in the context of the combined COPD assessment; Risk factors independent of disease stages were investigated.

### Inclusion Criterias

COPD over 40 years of age, having a smoking history of at least 10 years or more; COPD stability for at least 1 month ; having no acute infection; basic demographic features, pulmonary function test (PFT), body mass index (BMI), hemogram, CRP, albumin data; cholesterol, triglyceride, HDL, LDL, hemogram, CRP, albumin values taken in the outpatient follow-up visit; not taking lipid-lowering medications; no known atherosclerotic heart diseases; non-diabetic; without malignancy; additional cases without lung diseases, were included in the study (**Figure**).

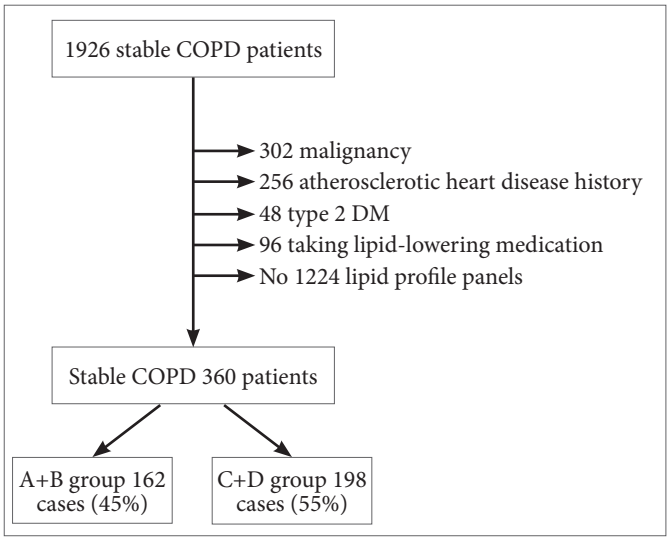


**Figure**. Patients flowchart

### Statistical Analysis

Kolmogrow-Smirnov or shapiro-wilk test was used for the distribution of all numerical values. Categorical data were evaluated with chi-square or fisher test, if appropriate, and numerical data with student t test or man-whitney-u test, if there are 2 groups, and with Anova or kruskal wallis if there are more than two groups. Independent risk factors affecting disease severity in our 2 main groups, which were determined as A+B group and C+D group, were analyzed by multivariate regression analysis. The model fit of the created regression analysis was evaluated with the hosmer and lemeshow test, and large values above 0.05 were considered significant. For all other p values in our study, values below $p<0.05$ were considered statistically significant. Analyzes were made using theinternational bussiness machines statistical package for the social sciences (IBM SPSS) 22 program. .

## RESULT

In our study, there were 360 cases, 293 (81.4%) of which were male. The mean age was 67.61±8.7 years. According to the combined COPD assessment, 37 cases (10.3%) were group A, 125 cases (34.7%) were group B, 20 cases (5.6%) were group C, and 178 cases (49.4%) were group D, while A+B group 162 was formed separately. cases (45%) and C+D group consisted of 198 cases (55%). As expected, the forced expiratory volume first second (FEV1) value was significantly lower in the C+D group ($p<0.0001$).

When potential confounding factors that may affect lipid values are excluded from the study; Other conditions such as age, gender, smoking characteristics, BMI, and hypertension were found to be similar in both study groups. Other spirometric and clinical features are in **Table 1**.

| Table 1: Basal features | | | | |
|---|---|---|---|---|
| **Characteristics** | **Total n=360** | **A+B group n=162 (45%)** | **C+D group n=198 (55%)** | **P value** |
| Age | 67.61±8.7 | 67.25±8.61 | 67.91±8.79 | P=0.47 |
| Gender | | | | P=0.062 |
| Male | 293 (81.4%) | 125 (77.2%) | 168 (84.8%) | |
| Female | 67 (18.6%) | 37 (22.8%) | 30 (15.2%) | |
| Smoking: | | | | P=0.089 |
| Quitted | 326 (90.6%) | 142 (87.7%) | 184 (92.9%) | |
| Still smoking | 34 (9.4%) | 20 (12.3%) | 14 (7.1%) | |
| GOLD | | | | P<0.0001 |
| 1 | 9 (2.5%) | 8 (4.9%) | 1 (0.5%) | |
| 2 | 119 (33.1%) | 70 (43.2%) | 49 (24.7%) | |
| 3 | 133 (36.9%) | 53 (32.7%) | 80 (40.4%) | |
| 4 | 99 (27.5%) | 31 (19.1%) | 68 (34.3%) | |
| Hypertension | | | | P=0.815 |
| Present | 56 (15.6%) | 26 (16%) | 30 (15.2%) | |
| Not present | 304 (84.4%) | 136 (84%) | 168 (84.8%) | |
| VKI (kg/m²) | 25.4±4.12 | 25.78±4.16 | 25.09±4.07 | |
| <25 | 190 (52.8%) | 86 (53.1%) | 104 (52.5%) | P=0.113 |
| ≥25 | 170 (47.2%) | 76 (46.9%) | 94 (47.5%) | P=0.915 |
| FEV1 | | | | |
| Liter | 1.22±0.56 | 1.39±0.62 | 1.08±0.46 | P<0.0001 |
| Percent | 43.75±17.86 | 49.33±19.12 | 39.18±15.35 | P<0.0001 |
| mMRC | | | | P<0.0001 |
| 0-1 | 60 (16.7%) | 38 (23.5%) | 22 (11.1%) | |
| 2 | 130 (36.1%) | 86 (53.1%) | 44 (22.2%) | |
| 3 | 90 (25%) | 33 (20.4%) | 57 (28.8%) | |
| 4 | 80 (22.2%) | 5 (3.1%) | 75 (37.9%) | |
| Hospitalisation/yr | 0.68±1.08 | 0(0%) | 1.24±1.19 | P<0.0001 |
| Exacerbation/yr | 2.01±2.62 | 0.25±0.43 | 3.44±2.78 | P<0.0001 |

As seen in **Table 2**, WBC, neutrophil, lymphocyte, NLR, monocytes, hemoglobin, CRP, Albumin, HDL, MHR were found to be different between the groups regarding statstical significance, while cholesterol, triglyceride, cholesterol and LDL levels were not at this level of significance.

As seen in **Table 3**; As a result of the combined COPD assessment; Independent risk factors were investigated in terms of disease stages. First, the model fit was evaluated with the hosmer and lemeshow test and it was found to be a suitable model (chi-square=6.44, p=0.598). Then, MHR, CRP and albumin values were found to be independent risk factors (**Table 3**) .

**Table 3.** Independent risk factors in COPD groups as a result of multivariate regression analysis

| **Characteristic** | **B** | **p-value** | **(95% GA)** | **Odds ratio** |
|---|---|---|---|---|
| MHR | 0.064 | P<0.0001 | 1.029-1.104 | 1.066 |
| CRP | 0.137 | P<0.0001 | 1.074-1.225 | 1.147 |
| Albumin | -0.077 | P=0.003 | 0.879-0.975 | 0.926 |

(Age, gender, smoking, hypertension, BMI, total cholesterol, triglyceride, HDL, LDL, MHR, CRP, Albumin values formed the model. The data were analyzed in terms of independent risk factors, including the dependent variable COPD group stages. The model fit was evaluated with the hosmer and lemeshow test, and it was observed as p=0.598 and chi-square test=6.44, indicating a good test fit.)

**Table 2.** Laboratory features

| **Characteristics** | **Total n=360** | **A+B group n=162(%45)** | **C+D group n=198(%55)** | **Pvalue** |
|---|---|---|---|---|
| WBC (×10³/µL) | 8.62±2.61 | 8.09±2.35 | 9.05±2.73 | P<0.0001 |
| Neutrophil (×10³/µL) | 4.07±4.28 | 2.9±1.72 | 5.03±5.37 | P<0.0001 |
| Lymphocyte (×10³/µL) | 1.89±0.78 | 2.01±0.74 | 1.78±0.8 | P=0.006 |
| NLR (%) | 4.07±4.28 | 2.9±1.72 | 5.03±5.37 | P<0.0001 |
| Monocytes (×10³/µL) | 0.66±0.30 | 0.58±0.24 | 0.72±0.33 | P<0.0001 |
| hemoglobin(g/dL) | 14.06±1.99 | 14.33±1.81 | 13.84±2.11 | P=0.022 |
| CRP (mg/L) | 4.26±4.25 | 3.07±3.09 | 5.22±4.81 | P<0.0001 |
| Albumin (g/L) | 38.91±6.54 | 40.66±5.19 | 37.48±7.17 | P<0.0001 |
| Cholesterol (mg/dL) | 187.97±46.58 | 192.12±43.3 | 184.58±48.94 | P=0.126 |
| Triglyceride (mg/dL) | 127.06±74.23 | 126±76.38 | 127.94±72.61 | P=0.805 |
| HDL (mg/dL) | 47.57±13.87 | 49.59±12.68 | 45.91±14.59 | P=0.012 |
| LDL (mg/dL) | | 117.16±37.9 | 114.02±38.94 | P=0.441 |
| Monosit/HDL (%) | 0.015±0.011 | 0.012±0.006 | 0.018±0.014 | P<0.0001 |

WBC=leukocytes, NLR= neutrophil lymphocyte ratio, CRP= C reactive protein, HDL=high-density lipoprotein, LDL=low-density lipoprotei

## DISCUSSION

In our study, we showed that high MHR rate, high CRP and low albumin values may be independent risk factors for high disease severity in our age, sex, and BMI-matched COPD groups. COPD is a chronic disease and the expected morbidity and morbidity increase with disease severity (1).

COPD is a systemic inflammatory disease and is often associated with comorbidities, and the persistence of inflammation may also lead to other diseases (3-5). In the study of Breyer et al. (5) in which patients with COPD and healthy controls and BMI of 25 and above were evaluated, they found the prevalence of metabolic syndrome to be high in the COPD group and they found a low mean HDL level in the copd group.

Features such as obesity and systemic steroid use may affect HDL values in patients with COPD (16). In this respect, we included patients who were in the stable period and did not need steroids and were matched in terms of BMI. In our sample group, the mean BMI was 25.4±4.12 and the male ratio was 80%, which is consistent with literature data (17-19). In addition, in our study, both groups were similar in terms of gender. HDL is a lipoprotein that carries cholesterol from non-hepatic cells to the liver. Low HDL values are a significant risk factor for atherosclerosis and cardiovascular diseases. HDL molecule shows antiatherogenic activity by regulating LDL oxidation. HDL has antiatherogenic effects as well as antioxidant and anti-inflammatory effects, and low HDL is usually associated with high LDL (6,7).

Monocytes are cell types that, during inflammation, interact with platelets and endothelial cells to release pro-oxidant and pro-inflammatory cytokines, thereby causing medial damage to smooth muscle cells, leading to differentiation, apoptosis, and increased oxidative stress (8,9). For this purpose, we analyzed the lipid profile, MHR, crp, albumin and hemogram data in terms of inflammatory markers that may be associated with the severity of COPD in our study. Smoking, hypertension and BMI, which could be potential confounding factors and affect inflammation, were similar in both groups, in other words, these conditions did not affect our data. Conditions that are likely to affect other significant lipid levels, such as malignancy, type 2 diabetes, and systemic steroid use were excluded from the study (20,6).

Smoking may also negatively affect HDL levels (21), but there was no difference between the groups in terms of smoking characteristics in our study (p=0.089). Zafirova-Ivanovska B et al. (16) in their study, they found high cholesterol and LDL values and low HDL values in the very severe COPD group in the lipid profile results they evaluated in severe and very severe COPD groups, but only the high cholesterol value reached the level of statistical significance. Markelic et al. (12) In their study with COPD and healthy controls, they found high monocytes, high MHR and high HDL values in the COPD group, and they also found a relationship between high MHR rate and more airway limitation. Yakar et al. (11) In their study with COPD and healthy controls, they found MHR to be high in the COPD group, but they found that it was not associated with the severity of the disease in the COPD groups. Nillawar et al. (13) In their study with COPD and healthy controls, they found that there was no difference between lipid profile values. Can, U., Yerlikaya In their study, they found that the HDL value was lower in the COPD group compared to the healthy controls, but they found that there was no difference in LDL, triglyceride and cholesterol values (14). Sariaydin GS. (15) found in their study lower HDL, higher triglyceride and higher CRP levels in the COPD group compared to healthy controls, while they found similar cholesterol and LDL levels. When we examine the lipid profile values in our groups that we have divided as COPD A+B and C+D in our current study; We found low HDL values in the C+D group ($p=0.012$), but we found similar cholesterol, triglyceride and LDL levels in this C+D group ($p>0.05$). We found high monocytes ($p<0.0001$), low albumin ($p<0.0001$) and high CRP ($p<0.0001$) values in the C+D group. Leukocyte, neutrophil, and NLR values were also found to be high in the C+D group, which is consistent with the literature data (22, 23). When we analyzed the severity of COPD disease in our study group to examine the independent risk factors with multivariate regression analysis as seen in Table 3, we found that the statistical significance levels of high MHR rate and CRP value and low albumin values continued in the C+D group.

The main limitations of our study are that it is a single-center and retrospective study. Although the BMI was found to be similar between the groups, the fact that the nutritional habits of the cases were not known is our other limitation.

## CONCLUSION

In our study, we think that high MHR rate, high CRP, and low albumin values in stable COPD patients may be a stimulant for increased disease severity. In our study, MHR, CRP and albumin values may vary in advanced COPD stages in stable COPD patients.

## ETHICAL DECLARATION

**Ethics Committee Approval:** This study was approved by the Health Sciences University Keçiören Education and Training Hospital Clinical Studies Ethics Board (Date: 22.03.2022, Decision No: 2012-KAEK-15/2490).

**Informed Consent:** Since the study was designed retrospectively, informed consent was not obtained from the patients.

**Conflict of Interest Status:** The authors declared that there was no conflict of interest in this study.

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

**Author Contributions:** All authors; declared that they participated in the design, execution, and analysis of the article and approved the final version.

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