doi: 10.53446/actamednicomedia.1143661

Acta Medica Nicomedia

Cilt: 6 Sayı: 1 Şubat 2023 / Vol: 6 Issue: 1 February 2023
https://dergipark.org.tr/tr/pub/actamednicomedia

Research Article | Araştırma Makalesi

DOES LOW MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION REALLY PREDICT MORTALITY IN ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE?

DÜŞÜK ORTALAMA KORPÜSKÜLER HEMOGLOBİN KONSANTRASYONU KRONİK OBSTRÜKTİF AKCİĞER HASTALIĞININ AKUT ALEVLENMELERİNDE MORTALİTEYİ GERÇEKTEN ÖNGÖRÜYOR MU?

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ABSTRACT

Objective: Several studies have shown low mean corpuscular hemoglobin concentration (MCHC) associations with mortality and poor clinical course in conditions associated with chronic inflammation, such as cardiac failure and COPD. Thus, this study aimed to determine the link between MCHC and readmission mortality in a large patient population with a minimum of 1 year of follow-up.

Methods: We recorded clinical data at admission, laboratory data, the number of admissions to the emergency room due to acute exacerbation of chronic obstructive pulmonary disease (AECOPD) following the discharge of the last patient recruited, the number of admissions to the pulmonology unit, and the number of intensive care unit admissions between 2018 and 2019. The follow-up duration ranged between 12 and 36 months.

Results: A total of 339 patients were included. Based on a ROC analysis, the cut-off value for MCHC was 32.35 g/dl. Comparison of clinical data according to this cut-off value showed an increase in the incidence of pneumonia during admission, hypercapnic respiratory failure, need for noninvasive mechanical ventilation (NIV), and the number of intensive care unit admissions within one year, as well as reduced survival in non-anemic subjects with MCHC ≤ 32.35 g/dL. In multivariate cox-regression analysis, MCHC was not an independent predictor of mortality risk.

Conclusion: We recommend careful monitoring and assessing comorbidities in acute exacerbation of COPD patients with low MCHC but without anemia. MCHC was not found to be an independent predictor of mortality, but there was a significant correlation between MCHC and survival in patients without anemia.

Keywords: COPD, MCHC, mortality, anemia

ÖZ

Amaç: Birkaç çalışma, düşük ortalama korpüsküler hemoglobin konsantrasyonunun (MCHC), kalp yetmezliği ve KOAH gibi kronik inflamasyonla ilişkili koşullarda mortalite ve kötü klinik seyir ile ilişkisini göstermiştir. Bu nedenle, bu çalışmada, minimum 1 yıllık takip süresi olan geniş bir hasta popülasyonunda MCHC ile yeniden yatış mortalitesi arasındaki bağlantıyı belirlemeyi amaçladık.

Yöntem: 2018 ve 2019 yılları arasında hastaneye kabul sırasındaki klinik veriler, laboratuvar verileri, kronik obstrüktif akciğer hastalığının akut alevlenmesi nedeniyle acil servise başvuru sayısı, göğüs hastalıkları ünitesine yatış sayısı ve yoğun bakım yatış sayısı, çalışmaya alınan son hastanın taburcu edilmesini takiben kaydedildi. Takip süresi 12 ile 36 ay arasında değişmekteydi.

Bulgular: Toplam 339 hasta dahil edildi. MCHC için eşik değeri 32.35 g/dl olarak bulundu. Bu cut-off değerine göre klinik verilerin karşılaştırılması yapıldı. 1 yıllık takip süresi içinde yeniden başvurularda pnömoni, hiperkapnik solunum yetmezliği, non-invaziv mekanik ventilasyon (NIV) ihtiyacı ve yoğun bakıma yatış sayısında artış olduğu gösterildi. Ayrıca MCHC ≤ 32.35 g/dL olan ve anemik olmayan kişilerde sağkalımın azaldığı gösterildi. Anemisi olmayan MCHC ≤ 32.35 g/dL grubunda artmış mortalite ile ilişkili faktörler incelendiğinde, ileri yaş, demans varlığı, karaciğer yetmezliği, 1 yıl içinde KOAH akut alevlenmesine bağlı acil servis başvuru sayısı, yoğun bakım ünitesi başvuru sayısı ve başvuru sırasında NIV ihtiyacı olduğu görüldü. Fakat kabul sırasında elde edilen MCHC değeri, mortaliteyi öngörmede bağımsız bir değişken olmadığı görüldü.

Sonuç: Düşük MCHC'li ancak anemisi olmayan KOAH akut alevlenmesi hastalarında diğer komorbiditelerin dikkatli bir şekilde izlenmesini ve değerlendirilmesini öneriyoruz. MCHC değeri, mortaliteyi öngörmede bağımsız bir değişken olmadığı görüldü ancak anemisi olmayan hastalarda MCHC ile sağkalım arasında anlamlı bir ilişki saptandı.

Anahtar Kelimeler: KOAH, MCHC, mortalite, anemi

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Submitted/Başvuru: 13.07.2022 • **Accepted/Kabul:** 22.01.2023 • **Published Online/ Online Yayın:** 28.02.2023

Introduction

COPD is the third leading global cause of death[1], with a trend toward progressively increasing mortality.[2] The most critical determinant of COPD mortality is the number of acute exacerbations during the disease.[3]
Approximately 10% to 30% of COPD patients have anemia[4], associated with reduced exercise capacity, perceived dyspnea, and need for oxygen support.[5] The purported causes of anemia in COPD include increased cytokine production due to chronic inflammation, iron deficiency, and anemia.[6,7] As a result of chronic inflammation, the incidence of cardiovascular diseases is also increasing, causing an increase in mortality. Baykal and Bulcun reported in their study that chronic hypoxemia in patients with COPD led to pulmonary vascular remodeling and increased pulmonary artery pressure.[8] In their study, Şahan and Bulut reported that as the clinical severity of COPD progresses, hypoxia increases, pulmonary hypertension appears, and some pathological changes occur in the right heart, which leads to atrial fibrillation.[9]
Only a few published studies offer insights into the relationship between COPD and iron deficiency. A cross-sectional study involving a multivariate analysis of lung capacity and serum nutrition parameters identified a direct link between the forced expiratory volume at 1 sec (FEV1) and serum iron levels.[10] MCHC is a hematological index of hemoglobin and total iron stores.[11,12] Studies have suggested that MCHC is a reliable parameter of functional iron status.[13]
In a study of 197 outpatients with chronic cardiac failure, Simbaqueba et al. showed that MCHC was a reliable prognostic indicator, particularly in those without anemia. These authors found a higher risk of mortality and increased admissions due to cardiac failure during a 5-year follow-up in patients with low MCHC. Such observations confirm the association between relatively low MCHC, chronic cardiac failure, and functional iron deficiency.[14] Again, Kento Sato et al. found higher 1-month mortality in AECOPD patients with low MCHC.[15]
The objective of this study was to evaluate the prognostic value of MCHC during the clinical course of AECOPD patients.

Methods

Study Population

All patients admitted to our tertiary chest diseases branch hospital were evaluated between January 2018 and January 2019 with AECOPD. AECOPD was defined as acute exacerbation, acute worsening of respiratory symptoms requiring antibiotic and or steroid therapy. According to the treatment they received and their clinical status, the patients were categorized into the following groups; mild acute exacerbation (no treatment), moderate acute exacerbation (steroid and or antibiotic therapy), severe acute exacerbation (steroid and or antibiotic therapy combined with noninvasive mechanical ventilation (NIV) for respiratory failure or the need for oxygen therapy). We recorded age, gender, and presence of obstructive sleep apnea syndrome (OSAS), hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), arrhythmia, dementia), thyroid dysfunction, cerebrovascular events, epilepsy, rheumatologic diseases, smoking history in all patients over 18 years of age hospitalized due to AECOPD. Also, we recorded the number of emergency room visits, hospital admissions, and intensive care unit admissions during a minimum one-year follow-up after discharge.
Survival of the patients was calculated by the difference between AECOPD and hospitalization and date of death. We determined mortality during a minimum follow-up of 1 year for all patients after the last recruited patient.
The study did not include patients with chronic heart failure, malignancy, interstitial lung disease, and inflammatory disease along with AECOPD. Among 491 patients who presented with AECOPD within a year, 70 had chronic heart failure, 74 patients had malignancy, four had interstitial lung disease, one had organized pneumonia, and one had acute cerebrovascular ischemia, and two patients had myotonic dystrophy. In total, 339 patients were included in the study. A hemoglobin level of < 13 g/dl and < 12 g/dl was considered diagnostic for anemia in male and female patients.
This study was designed to obtain data retrospectively. The ethics committee of Ankara Keçiören Training and Research Hospital approved this retrospective study. (Number of Approval: 2012-KAEK 15/2418; Date of Approval: November 9th, 2021).

Statistical Analysis

We used SPSS 22.0 (Statistical Program for Social Sciences) software package for statistical analysis. Kolmogorov Smirnov test was used to determine variables with normal distribution. The homogeneity of the variance was tested with Levene's test. For quantitative data, descriptive statistics such as arithmetic mean and standard deviation were presented for data with normal distribution and median (min-max) for data without normal distribution. Also, we provided frequencies and percentages for qualitative data. We compared comparisons between two independent groups with Student's t-test for normal distribution and Mann-Whitney U test for data without normal distribution. We compared qualitative data between the groups with chi-square or Fisher's exact test. Univariate and multivariate Cox regression analyses were carried out to determine the effect of risk factors on mortality. Cut-off values for the relationship between mortality and MCHC were identified using ROC under the curve analysis. Survival curves according to median MCHC and exacerbation severity were prepared using the Kaplan-Meier methodology, and log-rank tests were used to compare the groups. We evaluated the association between continuous variables with Spearman's correlation analyses. All statistical analyses were

performed at a 95% confidence interval and p-level of < 0.05.

Results

The mean age of 339 patients included in this study was 70.54, and 62.8% were male. The minimum follow-up period of the patient population was one year. Demographic data and comorbidities are shown in Table 1. The smoking histories of the patients were classified as active users, quitters, and non-smokers. According to this classification, 19.2% of the patients were active users, 52.4% quit, and 28.4% never smoked. The median hemoglobin value was 13.7 g/L (0.11-113.7). The median MCHC value was 31.8 g/dL (20.9-54.9). According to the ROC analysis to predict mortality (AUC=0.589, 95% CI:0.527-0.652, p=0.006), we found the best cut-off point of the MCHC value to be 32.35, the sensitivity of MCHC at this point was 75.4%, the selectivity was 40.6%, positive and negative predictive values were respectively; 42% and 75% (Figure 1).

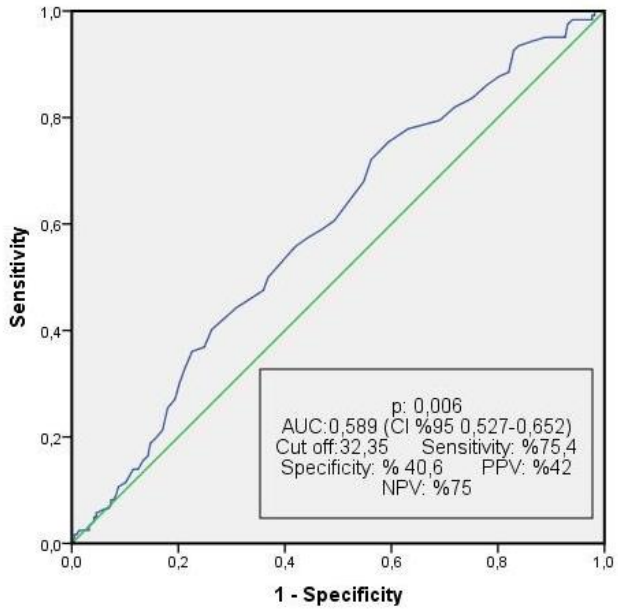

Figure 1. ROC curve of MCHC levels to predicting mortality

Table 1. Demographic characteristics of cases according to MCHC levels regarding the cut-off point obtained from ROC analysis

		TOTAL (n=339)	MCHC ≤ 32,35 (n=122)		MCHC > 32,35 (n=217)		p-value
		n (%)	n	%	n	%	
Gender	Female	126 (37.2%)	93	(42.1%)	33	(28.0%)	**0.010**
	Male	213 (62.8%)	128	(57.9%)	85	(72.0%)	
Age (year)		70.54 ± 10.86	71.20±10.64		66.93±11.22		0.122
Smoking History	None	96 (28.4%)	70	(31.7%)	26	(22.2%)	0.185
	Active	65 (19.2%)	41	(18.6%)	24	(20.5%)	
	Quit	177 (52.4%)	110		67	(57.3%)	
Diabetes Mellitus		107 (31.6%)	74	(33.5%)	33	(28.0%)	0.298
Hypertension		158 (46.6%)	103	(46.6%)	55	(46.6%)	0.999
Obstructive Sleep Apnea Syndrome		54 (15.9%)	36	(16.3%)	18	(15.3%)	0.804
Coronary Artery Disease		73 (21.5%)	46	(20.8%)	27	(22.9%)	0.659
Cardiac Arrhythmia		23 (6.8%)	15	(6.8%)	8	(6.8%)	0.998
Hypothyroid		7 (2.1%)	4	(1.8%)	3	(2.5%)	0.699
Pneumonia		268 (79.1%)	183	(82.8%)	85	(72.0%)	**0.020**
Bronchiectasis		105 (31.0%)	62	(28.1%)	43	(36.4%)	0.112
Anemia		101 (29.8%)	75	(33.9%)	26	(22.0%)	0.022
Moderate Liver Failure		27 (8%)	20	(9.0%)	7	(5.9%)	0.339
Severe Liver Failure		3 (0.9%)	3	(1.4%)	-	-	
Moderate-Severe Kidney Failure		71 (20.9%)	44	(19.9%)	27	(22.9%)	0.522
MCHC level		31.8 (20.9-54.9)	-	-	-	-	-

MCHC: Mean corpuscular hemoglobin concentration

There was a statistically significant difference in long-term mortality between the groups with MCHC higher and lower than 32.35 g/dL (p<0.001). Accordingly, we found the mortality rate higher for the group with MCHC≤ 32.35 g/dL (p<0.011).

MCHC less than 32.35 is associated with mortality in patients who had emergency admissions in the previous year. MCHC less than 32.35 is associated with mortality in patients who have had acute exacerbations in the previous year. For last year, there was no statistically significant relationship between the MCHC cut-off value

and mortality in AECOPD patients admitted to the intensive care unit. For the group with MCHC≤32.35, the incidence of hypercapnic respiratory failure ($PaCO_2$> 45 mmHg) (p<0.001), the rate of noninvasive mechanical ventilation use during hospitalization (p<0.001), the rate of admission to intensive care unit within one year (p=0.002) and pneumonia incidence (p=0.020) were found to be higher compared to the group with MCHC>32.35 (Table 2).

Table 2. Clinical characteristics of cases according to MCHC levels regarding the cut-off point obtained from ROC analysis

Clinical characteristics of the patients	TOTAL (n=339)		MCHC ≤ 32.35 (n=221)		MCHC > 32.35 (n=118)		p
	n	(%) or mean (min-max)	n	(%) or mean (min-max)	n	(%) or mean (min-max)	
Moderate COPD Acute Exacerbation	18	5.3%	10	4.5%	8	6.8%	0.378
Severe COPD Acute Exacerbation	321	94.7%	211	95.5%	110	93.2%	
Acute Hypercapnic Respiratory Failure	60	17.7%	45	20.4%	15	12.7%	0.079
Chronic Hypercapnic Respiratory Failure	279	82.3%	176	79.6%	103	87.3%	
Admissions to Emergency Service within 1 Year	304	89.7%	201	66.1%	103	33.9%	**0.001****
Admissions with Acute Exacerbation of COPD within 1 Year	334	98.5%	218	65.3%	116	34.7%	**0.002****
Admissions to the Intensive Care Unit with Acute Exacerbation of COPD within 1 Year	52	15.3%	44	84.6%	8	15.4%	0.129
Decompensated Respiratory Failure in Arterial Blood Gas at Admission (pH<7.35)	57	17.0%	43	19.6%	14	12.0%	0.074
Hypercapnic Respiratory Failure in Arterial Blood Gases at Admission ($PaCO_2$> 45 mmHg)	145	42.8%	113	51.1%	32	27.1%	**<0.001**
Hemoglobin levels (g/dL)	-	13.6 (8.30-21.1)	-	13.3 (8.30-18.3)	-	14.2 (10.2-21.1)	**0.001**
Survival duration (months)	-	30 (1-39)	-	29 (1-39)	-	31 (1-39)	**0.011**
Use of nasal oxygen therapy during hospitalization	319	94.1%	210	95%	109	92.4%	0.324
Use of NIV therapy during hospitalization	92	27.1%	75	33.9%	17	14.4%	**<0.001**

COPD: Chronic Obstructive Pulmonary Disease
NIV: Noninvasive Mechanical Ventilation

There was a significant correlation between MCHC and survival in patients without anemia (p=0.005). Table 3 shows the results of univariate Cox proportional hazards regression analysis for all possible factors thought to have an impact on overall survival. Univariate analysis showed associations between mortality and advanced age (HR=1.030, 95% CI:1.012-1.048, p=0.001), dementia (HR=4.539, 95%CI:1.845-11.167, P=0.001), pneumonia (HR=1.828, 95% CI: 1.095-3.051, P=0.021), liver failure (HR=1.999, 95% CI: 1.212-2.298, P=0.007), higher number of admissions due to AECOPD within a 1-year period (HR=1.082, 95%CI:1.009-1.160, p=0.027), more prolonged stay at intensive care unit due to acute exacerbation of COPD within a 1 year period (HR=1.354, 95% CI: 1.172-1.563, p<0.001), use of NIV at admission (HR=1.759, 95% CI:1.217-2.541, p=0.003), and MCHC ≤ 32.35 (HR=0.559, 95% CI: 0.370-0.844, p=0.006).

We fitted values associated with mortality in the univariate cox regression analysis into multivariate cox regression models. This analysis showed that advanced age, dementia, liver failure, increased emergency unit visits and ICU admissions due to COPD exacerbation within one year, and increased need for NIV during admission was associated with mortality. At the same time, MCHC was not an independent predictor of mortality (Table 4).

Discussion

MCHC is a hematologic laboratory parameter utilized for diagnosing and monitoring patients with iron deficiency anemia and measuring the oxygen-carrying capacity of red blood cells.[13,16]

Iron deficiency associated with chronic inflammation is a known indicator of poor long-term prognosis, independent of anemia.[17] Median Hg in our patient group was 13.7 g/dL, and MCHC was 31.8 g/dL. Overall, 101 patients were found to have anemia. However, we did not measure serum iron levels in our participants. According to our observations, MCHC had prognostic significance in patients without anemia.

Table 3. Univariate cox regression analysis to identify variables that predict survival in patients with chronic obstructive pulmonary disease with acute exacerbation

Univariate Cox Regression	Wald	p	HR	95% CI for HR
Age	11.079	**0.001**	1.030	(1.012-1.048)
Sex (ref: Female)	0.083	0.774	0.948	(0.658-1.365)
Smoking History	1.411	0.235	0.743	(0.455-1.213)
MCHC	5.613	**0.018**	0.907	(0.837-0.983)
Diabetes Mellitus	0.219	0.640	1.094	(0.751-1.593)
Hypertension	0.017	0.896	1.024	(0.718-1.462)
Obstructive Sleep Apnea Syndrome	3.918	**0.048**	0.559	(0.315-0.994)
Coronary Artery Disease	0.058	0.809	0.947	(0.610-1.470)
Arrhythmia	0.531	0.466	1.272	(0.666-2.429)
Dementia	10.844	**0.001**	4.539	(1.845-11.167)
Pneumonia	5.317	**0.021**	1.828	(1.095-3.051)
Bronchiectasis	0.929	0.335	0.824	(0.557-1.221)
Presence of Liver Failure	7.351	**0.007**	1.999	(1.212-2.298)
Hypercapnic Respiratory Failure (ref:acute)	1.239	**0.266**	0.782	(0.507-1.206)
Number of admissions to the emergency service within 1 year	3.282	0.070	1.011	(0.999-1.023)
Number of admissions with acute exacerbation of COPD within 1 year	4.883	**0.027**	1.082	(1.009-1.160)
Number of admissions to the intensive care unit with acute exacerbation of COPD within 1 year	17.014	**<0.001**	1.354	(1.172-1.563)
Arterial Blood Gas HCO_3 at Admission	0.016	0.416	1.013	(0.982-1.045)
Arterial Blood Gas at Admission (ref: decompensated)	1.321	0.250	0.773	(0.497-1.200)
Arterial Blood Gas at Admission (ref: $PaC0_2$>45)	2.240	0.134	1.312	(0.919-1.871)
Acute exacerbation (ref: moderate acute exacerbation)	0.017	0.896	0.950	(0.443-2.039)
Hemoglobin	1.775	0.183	1.019	(0.991-1.047)
Anemia	5.804	**0.016**	1.569	(1.088-2.262)
Nasal Oxygen Use during Hospitalization	0.041	0.839	1.082	(0.504-2.321)
Use of NIV during Hospitalization	9.031	**0.003**	1.759	(1.217-2.541)

Wald: test statistics, HR: hazard radio, Statistically significant p-values are in bold.

Table 4. Multivariate cox regression analysis applied to identify variables that predict survival in patients with chronic obstructive pulmonary disease with acute exacerbation

Multivariate Cox Regression	Wald	p	HR	95% CI for HR
Model 1				
Age	12.368	**<0.001**	1.033	(1.014-1.051)
Sex (ref: Female)	0.466	0.495	1.140	(0.783-1.659)
MCHC	6.936	**0.008**	0.894	(0.823-0.972)
Model 2				
Age	8.587	**0.003**	1.028	(1.009-1.048)
Sex (ref: Female)	2.151	0.142	1.335	(0.907-1.963)
MCHC	3.639	0.056	0.921	(0.846-1.002)
Dementia	5.199	**0.023**	3.013	(1.168-7.778)
Pneumonia	3.631	0.057	1.657	(0.986-2.785)
Presence of Liver Failure	7.777	**0.005**	2.068	(1.241-3.447)
Anemia	3.210	0.073	1.413	(0.968-2.062)
Model 3				
Age	18.738	**<0.001**	1.043	(1.023-1.063)
Sex	0.216	0.642	1.095	(0.746-1.609)
MCHC	5.770	**0.016**	.905	(0.834-0.982)
Number of admissions to the emergency service within 1 year	8.868	**0.003**	1.140	(1.046-1.243)
Number of admissions to the intensive care unit with acute exacerbation of COPD in 1 year	15.004	**<0.001**	1.367	(1.167-1.602)
Model 4				
Age	16.688	**<0.001**	1.040	(1.021-1.060)
Sex	1.732	0.188	1.295	(0.881-1.902)
MCHC	3.310	0.069	0.927	(0.854-1.006)
Use of NIV during Hospitalization	11.344	**0.001**	1.991	(1.334-2.973)

Wald: test statistics, HR: hazard radio, Statistically significant p-values are in bold.

In a study by Huang et al., low MCHC in patients admitted to the intensive care unit following acute myocardial infarction was associated with an increased risk of in-hospital mortality.[18] In another study from 2013 by Simbaqueba et al.[14] involving patients with systolic heart failure, those with lower MCHC had an elevated risk of death and transplantation and an increased likelihood of hospitalization due to heart failure.

In the study of Kento Sato et al. for patients followed up with COPD acute exacerbation, a correlation was found between low MCHC value and 30-day mortality.[15] They included 195 AECOPDs patients and a one-month follow-up period for assessing mortality. We enrolled 339 patients in our study, with a follow-up period of 1-3 years.

This study investigated the prognostic value of MCHC for patients treated in the hospital (intensive care, emergency, or chest disease ward) due to AECOPD. When the patients were examined according to the determined cut-off value (32.35 g/dL), we found the survival duration lower for the group with MCHC≤32.35 g/dL. For patients with MCHC≤32.35, the incidence of hypercapnic respiratory failure during hospitalization ($PaCO_2$>45 mmHg), the rate of noninvasive mechanical ventilation use during hospitalization, the rate of admission to intensive care unit within one year, and pneumonia incidence were found to be higher. In our Cox regression analysis, MCHC did not appear to be a strong predictor of mortality risk, contrasting with many other reports. Despite a large sample size, this might have resulted from several factors, such as the retrospective design of our study, confounding factors inherently present in AECOPD, and lack of accurate information on whether AECOPD caused each death. Further prospective studies may be required to elucidate better the association between MCHC and mortality in this setting.

MCHC ≤ 32.35 g/dL was statistically significant in determining the overall survival (OS) value in our ROC analysis of MCHC measurements in estimating the survival duration. When we compared the MCHC cut-off values with other studies, we inferred that the cut-off value was similar to our research's. Simbaqueba et al. reported that the patients whose MCHC was 32.7 g/dL and below had the worst prognosis.[14] In a 2016 paper, Huang et al. reported that patients with an MCHC < 32.8 g/dl had an increased risk of in-hospital death.[18] In the study of Kento Sato et al., the MCHC cut-off value was 31.6 g/dL.[15] In our study, the MCHC cut-off value was 32.35.

In our multivariate regression models, factors associated with a significantly increased mortality risk at one year included advanced age, dementia, liver failure, a higher number of emergency room visits and ICU admissions due to COPD exacerbations during one year, and NIV use. These findings support that low MCHC may indicate poor outcomes in AECOPD patients.

One of the most important limitations is that our study is a mono-centered, retrospective data analysis and lacks a common cut-off value that we can compare. Due to the study's retrospective nature, we could not obtain serum iron levels because it isn't done regularly.

Future studies will investigate whether the MCHC value is an effective biomarker in determining the indication for intensive care hospitalization and the use of NIV in patients followed up with AECOPD. A second study should examine the association between the predictive power of MCHC and infection and determine their ability to distinguish non-bacterial AECOPD from bacteria.

Patients with AECOPD often admit to emergency services. A Hemogram examination is among the first laboratory tests requested in the emergency admissions of these patients. It is cheap and easy to access. The study's most vital feature is its exclusion of the cases with malignancy and chronic heart failure known to affect the MCHC value and its comparatively larger sample size and longer follow-up vs. most previous studies.

Conclusion

Our results showed an increased risk of ICU admission, hypercapnic respiratory failure, need for ICU use, and pneumonia among patients with lower MCHC. Clinicians should pay adequate attention to low MCHC levels among AECOPD patients regardless of anemia.

Compliance with Ethical Standards

Health Sciences University Keçiören Education and Research Hospital, Clinical Studies Ethic Board Decision date: 09.11.2021, Decision number:2012-KAEK-15/2418.

Conflict of Interest

The authors declare no conflicts of interest.

Author Contribution

Authors contributed equally to this work.

Financial Disclosure

Financial disclosure none.

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