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Evaluation of the relationship between carbon monoxide levels and neutrophil/lymphocyte ratios and platelet/lymphocyte ratios in smokers

NURCAN AKBAS GUNES[A–G], DUYGU CELIK[B, D, E, G]
ORCID ID: 0000-0001-8688-5839 ORCID ID: 0000-0001-9160-267X

Department of Family Medicine, Faculty of Medicine, Bolu Abant Izzet Baysal University, Bolu, Turkey

A – Study Design, **B** – Data Collection, **C** – Statistical Analysis, **D** – Data Interpretation, **E** – Manuscript Preparation, **F** – Literature Search, **G** – Funds Collection

Summary **Background.** Smoking is the most dangerous modifiable risk factor all over the world and requires the lowest cost to quit.
Objectives. In this study, we aimed to determine the relationship between the Fagerström Test for Nicotine Dependence (FTND) and carbon monoxide (CO) levels and neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), monocyte/lymphocyte ratio (MLR) and RDW, WBC, MPV values.
Material and methods. 138 participants who applied to the Smoking Cessation Clinic of Bolu Izzet Baysal Training and Research Hospital between January 2022 and March 2022 were included in our study. After obtaining the necessary consent, the FTND test and CO levels in expiratory air were measured. The required haematological values of the participants were evaluated.
Results. It was found that there was statistical significance between the CO levels of the participants and their FTND scores, and it was observed that the FTND scores increased as the CO level increased ($p = 0.000$). There was a statistically significant correlation between CO levels and PLR ratios and WBC levels ($p = 0.024$, $p = 0.000$). It was determined that as the CO level increased, the PLR ratios decreased, and the WBC values increased.
Conclusions. In our study, a positive correlation was found between FTND levels and exhaled CO levels. We can say that CO levels can be a marker in predicting the level of addiction. In addition, it was observed that there was a significant relationship between exhaled CO levels and FTND levels, as well as PLR and WBC values.
Key words: carbon monoxide, smoking, blood platelets, monocytes, lymphocytes.

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Background

Tobacco use, which is increasing day by day, is one of the most important public health problems that threaten human and public health. According to the World Health Organization (WHO), 4 million people die every year due to diseases caused by tobacco use [1]. As in the world, tobacco use in our country is increasing day by day and causes many diseases in people who use it. Although tobacco is used in many forms, it is most often consumed in the form of cigarettes. It is the most widely used and the most dangerous modifiable risk factor, though requiring a low cost to be discontinued, whose relationship with atherosclerosis has been proven most definitively [2]. Cigarette smoke contains more than 4000 substances, such as nitrosamines, aromatic hydrocarbons, ammonia, hydrogen cyanide, carbon monoxide (CO) and nicotine. The nicotine it contains is addictive to users. In cigarette addiction, in addition to nicotine, psychological factors and habits also play a role [3].

Various tools are used to assess nicotine addiction in smokers. One of these tools is the Fagerström Test for Nicotine Dependence (FTND). In studies, the measurement of the CO level in the expiratory air is also a very important biomarker in the diagnosis, treatment and follow-up stages of smoking addiction [4]. In addition, the level of CO in the expiratory air can distinguish smokers and non-smokers with 83% specificity and 95% sensitivity [5]. Many studies have been conducted examining the relationship between the level of CO in expiratory air and the severity of nicotine addiction [4–6]. Therefore, in this study, we wanted to evaluate whether there is a relationship between FTND levels and CO levels.

Smoking accelerates the atherosclerotic process with a wide variety of mechanisms. It increases platelet aggregation, decreases myocardial oxygen use and causes hypoxia in vascular structures with an increase in carbon monoxide level. It contributes to the formation and progression of atheroma plaques in the intima through the oxidation of lipids. In the same study, the amount of LDL and total cholesterol in smokers showed significant differences compared to non-smokers. Carotid intima thickness, which is one of the earliest signs of atherosclerosis, was found to be significantly higher in smokers compared to non-smokers [6].

Neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR) and monocyte/lymphocyte ratio (MLR) have been associated with many diseases. It has been shown that they are associated with the prognosis in patients with pulmonary embolism [7], they are some of the independent factors affecting disease activity in patients with rheumatoid arthritis [8], and they also reflect the inflammatory response and disease activity in SLE patients. All these studies in recent years show us that the ratios of NLR, PLR and MLR have not yet been clarified.

Objectives

In this study, we aimed to determine the relationship between FTND levels and CO levels, NLR, PLR, MLR ratios and

RDW, WBC, MPV values in individuals with an addiction to smoking. Thus, we will have the opportunity to find an answer to the question of whether we can use these haematological parameters to predict the severity of addiction.

Material and methods

Study design

For the study, first of all, necessary permission was obtained from the local ethics committee (2020/57). This study was designed as a cross-sectional descriptive study. It was carried out in accordance with the Declaration of Helsinki.

Patients who applied to the Smoking Cessation Outpatient Clinic of Bolu Izzet Baysal Training and Research Hospital between January 2022 and March 2022 were included in our study. After obtaining the necessary consent, the CO levels in the expiratory air were measured and the questionnaire form, which was created by scanning the relevant literature, was applied to the participants in a face to face setting. Patients with comorbidities and a history of continuous drug use were excluded from our study. Participants over the age of 18, who did not have any additional disease and who agreed to participate in our study were included in our study. The laboratory results of the patients recorded in the hospital information management system were evaluated.

Data collection tools

The patient information form was created by the authors by scanning the relevant literature. It included the participants' age, gender, socio-economic status, marital status, how many years and how many cigarettes they smoked per day.

The Fagerström Test for Nicotine Dependence (FTND) was used to measure the participants' degree of nicotine dependence. Its validity and reliability test was performed in Turkey and Cronbach's alpha value was found to be 0.56 [9]. Scores from the scale were categorised as 0–2 very low, 3–4 low, 5 moderate, 6–7 high and 8–10 very high.

Measurement of CO levels in the expiratory air is a marker used in the diagnosis and treatment of addiction in smokers. Measurements were made using the TABATABA device.

Statistical analysis

SPSS Windows version 25.0 was used for statistical analysis of the data. Arithmetic mean ± standard deviation was calculated for numerical data. Data specified as attributes was expressed as a percentage (%). The *t*-Test and Mann-Whitney U test were also used for statistical evaluation. A value of $p < 0.05$ was considered statistically significant.

Results

A total of 138 participants took part in our study. Their ages were in the range of 41.57 ± 13.37 (min: 19, max: 68). 41.3% ($n = 57$) of the participants were female, and 58.7% ($n = 81$) were male. 76.1% ($n = 105$) of the participants were married, and 23.9% ($n = 33$) were single. When the socio-economic status of the participants was evaluated, 82.6% ($n = 114$) were found to be at a medium level.

The mean exhaled CO level was found to be 10.57 ± 6.31. When the number of pack years of smoking was evaluated, as the total was 26.26 ± 18.31.

When the CO levels of the participants and the differences between the genders were evaluated, no statistically significant difference was found ($p = 0.760$). In addition, when the CO levels of spouses, co-workers and smokers were evaluated, there was no statistically significant difference ($p = 0.703$, $p = 0.519$). No statistical significance was found when marital status and CO levels were compared ($p = 0.541$).

In the statistical comparison between the CO levels of the participants and NLR, PLR, MLR, and MPV, RDW, WBC values, a statistically significant relationship was found between PLR and WBC levels ($p = 0.024$, $p = 0.000$). In the statistical comparison between FTND scores and haematological parameters, a statistically significant relationship was found between PLR and WBC levels ($p = 0.000$, $p = 0.005$). The statistical relationship with other parameters is shown in Table 1.

When the relationship between the FTND levels of the participants and the haematological parameters was evaluated, it was found that there was a positive correlation between the WBC values and a negative correlation between the PLR. As FTND scores increase, WBC values increase, and PLR decrease ($p = 0.001$, $p = 0.002$) (Table 2).

Table 1. Evaluation of the participants' CO and FTND scores and haematological parameters

		NLR	PLR	MLR	MPV	RDW	WBC	FTND scores	CO levels	How many packs/year	Age
FTND scores	*r*	-.164	-.308**	-.103	.020	.083	.240**		.523**		
	p	0.054	**0.000**	0.227	0.820	0.332	**0.005**		0.000		
CO levels	*r*	.077	-.192*	-.009	-.001	-.086	.372**	.523**		.492**	.122
	p	0.367	**0.024**	0.917	0.988	0.318	**0.000**	**0.000**		**0.000**	.155

* Carbon monoxide (CO) levels and neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), monocyte/lymphocyte ratio (MLR), Fagerström Test for Nicotine Dependence (FTND), ** Pearson Correlation Analysis.

Table 2. Detailed examination of the participants' FTND levels and haematological parameters

	FTND scores	Mean	Std. Deviation	*p*	95% Confidence Interval of the difference	
					Lower	Upper
NLR	Low	2.22	1.15	0.462	-0.27	0.60
	High	2.06	1.18			
PLR	Low	137.57	41.88	**0.001**	11.67	46.92
	High	108.27	48.78			
MLR	Low	0.32	0.16	0.898	-0.06	0.07
	High	0.32	0.20			

Table 2. Detailed examination of the participants' FTND levels and haematological parameters						
	FTND scores	Mean	Std. Deviation	*p*	95% Confidence Interval of the difference	
					Lower	Upper
WBC	Low	7.28	1.50	**0.002**	-2.03	-0.47
	High	8.53	2.29			
RDW	Low	14.47	1.75	0.384	-0.31	0.80
	High	14.23	1.30			
MPV	Low	8.90	1.58	0.380	-0.83	0.32
	High	9.16	1.50			

*Neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), monocyte/lymphocyte ratio (MLR), Fagerström Test for Nicotine Dependence (FTND), **Low *n*: 42, High *n*: 78.

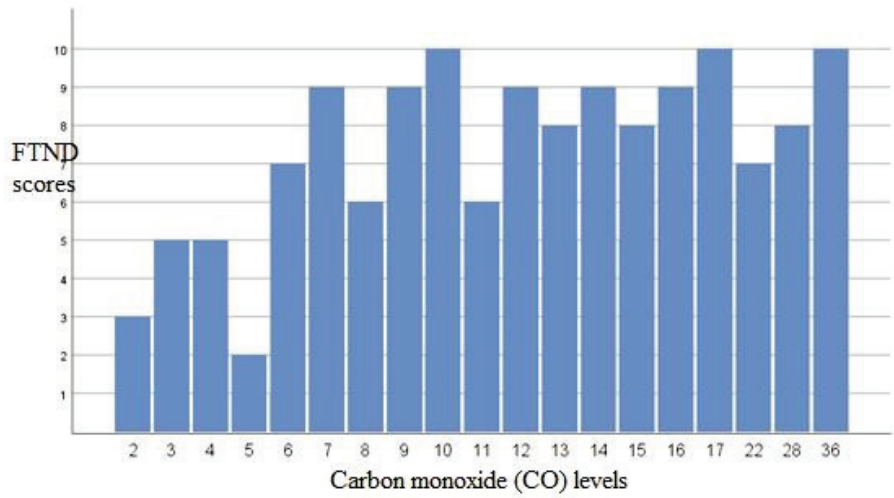

Figure 1. Relationship between the CO levels of the participants and their Fagerström Test for Nicotine Dependence (FTND)

A statistical significance was found in the statistical comparison between CO levels and FTND scores, and it was observed that FTND scores increased as the CO level increased ($p = 0.000$) (Figure 1).

Discussion

Smoking is known to be associated with cardiovascular diseases, metabolic syndrome, hypertension, coronary artery diseases and respiratory tract pathologies [10, 11]. Studies have also shown the effects of smoking on the haematopoietic system [10, 12, 13]. The number of studies showing the relationship between CO levels and FTND levels and the ratios of NLR, PLR and MLR is limited. The question of whether measurement of exhaled CO can be used instead of the FTND test remains to be answered. In addition, the relationship between CO levels and blood NLR and PLR ratios is another question to be answered.

In a study performed on nicotine-dependent men in Malaysia, a positive correlation was found between FTND scores and exhaled CO levels [14]. In a study conducted in India, it was shown that exhaled CO levels can be a marker for nicotine addiction [15]. In another study, it was stated that exhaled CO levels can be used in cases where there is no confidence in the answers to FTND questions [16]. Despite these, a study conducted in Austria concluded that exhaled CO levels can be used to detect smoking status but cannot be an indicator of nicotine addiction [17]. In our study, it was observed that FTND scores increased as CO levels increased. Considering the results obtained from our study, it can be concluded that exhaled CO levels can be used to evaluate nicotine addiction. In addition to FTND, we can say that exhaled CO is suitable in daily practice, and it is inexpensive and easy to apply in evaluating nicotine addiction in our country. The results from different countries also show that new studies are needed to reach clarity on this issue.

In a study conducted on smokers, no difference was observed when the relationship between smoking levels and NLR and PLR ratios was evaluated. Differences were found in RDW, MPV and platelet counts [17]. In a study conducted in our country, it was found that NLR increased and PLR decreased in smokers [18]. In our study, there was no difference between CO and FTND levels, NLR, MLR ratios and RDW and MPV values. There was a significant difference between the exhaled CO and FTND levels and the PLR ($p = 0.000$). It was observed that PLR ratios decreased as CO and FTND levels increased. Different studies involving large populations are needed on this subject.

In a study on the WBC values of individuals who quit smoking, it was determined that WBC values decreased in those who quit smoking after treatment compared to those who did not quit, and this decrease was attributed to the decrease in inflammation caused by smoking [19]. In a study conducted in India, it was observed that WBC values increased as smoking levels increased [20]. In our study, it was determined that WBC values increased as CO and FTND levels increased. Increased inflammation may have caused an increase in WBC values.

In a study conducted in India, the mean exhaled CO level was found to be 15.6 ± 7.0 [21]. In a study evaluating the exhaled CO levels of healthy smokers in the province of Elazig in Turkey, the mean CO level was measured as 17.13 ± 8.50 [22].

In our study, this value was found to be 10.57 ± 6.31. Average CO levels vary between different countries and individuals living in different regions of the same country. Air pollution and other influencing factors also need to be evaluated.

One of the limitations of our study is that it was conducted in a single centre. We cannot generalise the results of our study. The answers given by the participants to the survey questions were taken into account. It is not possible to be completely sure of the reliability of the answers to the questions given by the participants.

Conclusions

In our study, a positive correlation was found between FTND levels and exhaled CO levels. We can say that CO levels are a marker in predicting the level of addiction. In addition, it was observed that there was a significant relationship between exhaled CO levels and FTND levels, as well as PLR and WBC values. We can use these ratios in addition to the CO and FTND levels to predict addiction levels. There is a need for different studies concerning this subject in large populations.

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Tables: 2
Figures: 1
References: 22

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Address for correspondence:
Nurcan Akbas Gunes, MD
Kılıçarslan Neighborhood
Orhangazi Street, Number 21/B/6
Bolu
Turkey
Tel.: +90 5054929079
E-mail: drnurak@hotmail.com