The effects of smoking cessation on the ratios of neutrophil/lymphocyte, platelet/lymphocyte, mean platelet volume/lymphocyte and monocyte/high-density lipoprotein cholesterol

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ABSTRACT

Abstract. The amount of smoking, level of smoking addiction and smoking cessation have effects on blood cells, blood lipid levels, neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), mean platelet volume (MPV)/lymphocyte ratio (MPVLR) and monocyte/high-density lipoprotein (HDL) ratio (MHR).

Methods. In this self-controlled experimental study, we included individuals who applied to a smoking cessation clinic and quit smoking. Their sociodemographic and clinical characteristics, the amount of cigarettes consumed (pack/year), their Fagerstrom test for nicotine dependence (FTND) results, haemogram values before and 6 months after quitting smoking, NLR, PLR, MPVLR, MHR and blood lipid levels before and after the treatment were compared retrospectively.

Results. The mean (SD) age of the 239 individuals who participated in the study was 41.7 (10.9) years and 55.2% of them were women. Their mean FTND score was 7.06 (2.0), and most of them (47.7%) had a very high level of addiction. After the smoking cessation treatment, their neutrophil, platelet, MPV, red cell distribution width, platelet distribution width (PDW), cholesterol, triglyceride, low-density lipoprotein, NLR, PLR, MPVLR, MHR and HDL values increased ($p < 0.05$). The amount of smoking and level of dependence were negatively correlated with HDL, and positively correlated with other parameters.

Conclusion. After smoking cessation, in addition to dyslipidaemia, the NLR, PLR, MPVLR and MHR values also decreased, and the difference was found to correlate with the level of addiction and the amount of smoking.

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INTRODUCTION

Cigarette smoking is an important and independent risk factor for atherosclerosis, coronary artery disease, peripheral vascular disorders, cancer, etc.[1] It is assumed that the negative effects of smoking are due to the changes in inflammation, oxidative stress, antithrombotic and fibrinolysis systems.[2] It is known that smoking has negative effects on the haematopoietic system and lipid parameters, and many studies have shown that smoking causes an increase in haemoglobin, haematocrit, leucocyte, eosinophil and platelet levels in peripheral blood and lipid parameters except high-density lipoprotein (HDL).[1,3] Nicotine increases the release of catecholamines and steroids from the adrenal gland, causing an increase in the number of leucocytes. The inflammation caused by the tissue destruction effect of cigarette smoke on the lung parenchyma also contributes to the increase in leucocyte levels.[4]

Studies have shown that the levels and proportions of cells (e.g. leukocytes, neutrophils, thrombocytes) such as complete blood count can be used as a marker in the detection of systemic inflammation, which is known to play a role in the pathogenesis of many diseases. Neutrophil/lymphocyte ratio (NLR) is a combined marker obtained by the use of absolute neutrophil and lymphocyte counts.[5] Platelet/lymphocyte ratio (PLR), which is the combination of both parameters, is seen as a mortality determinant in cardiovascular and lung diseases and some malignant diseases.[6] PLR provides insight into aggregation and inflammation pathways and is considered more valuable than either platelet or lymphocyte count alone in predicting coronary atherosclerotic burden. Therefore, these markers are used as effective, simple and inexpensive laboratory parameters for the diagnosis and prognosis of coronary artery disease even in asymptomatic individuals.[7]

Mean platelet volume (MPV) is a potential marker of platelet activation and MPV levels are elevated in thromboembolic diseases.[8] Many studies have shown that MPV/lymphocyte ratio (MPVLR) is also a negative inflammatory marker in cardiovascular diseases and some malignant diseases.[9,10] Red cell distribution width (RDW) is an indicator of the size of erythrocytes, and it has been reported that, in addition to the differential diagnosis of anaemia, it can be used as a mortality indicator in acute heart failure, pulmonary embolism, acute myocardial infarction, peripheral artery disease and acute renal failure in the general population.[11]

Monocyte/HDL ratio (MHR) is a new cardiovascular

prognostic marker reported in recent studies.[12] It has also been reported that the MHR rate is higher in smokers compared to non-smokers and the degree of this increase correlates positively with the duration and amount of smoking.[13]

Some studies have examined the effects of smoking on the haemostatic, fibrinolytic, antioxidant and haematological systems, and compared smokers and non-smokers in this regard. However, to the best of our knowledge, no study has investigated the effects of cessation of smoking on NLR, PLR, MPVLR and MHR values in individuals who quit smoking. We investigated the changes in haemogram values, blood lipid levels and NLR, PLR, MPVLR and MHR values in smokers after cessation of smoking.

METHODS

In this self-controlled experimental study, we included individuals who enrolled at the smoking cessation outpatient clinic of the Family Medicine Department, Training and Research Hospital, Karabuk University between January and December 2018. Their sociodemographic and clinical characteristics such as age, gender, education, employment status, history of alcohol use and comorbid illness, and the amount of cigarettes they consumed (pack/year), their Fagerstrom test for nicotine dependence (FTND) results, haemogram values before and 6 months after cessation of smoking, NLR, PLR, MPVLR, MHR and blood lipid levels were retrospectively obtained from the patient files and hospital automation system. Those with missing data in their files and blood tests, those who did not come for follow-up and who could not quit smoking were not included in the study. The parameters were evaluated in terms of the amount of cigarettes smoked, the level of addiction, and whether there were any changes before and after cessation of smoking.

FTND is a widely used scale for determining nicotine addiction. It consists of 6 questions which yield a total score where 0–2 points refer to very low addiction, 3–4 points to low addiction, 5 points to medium addiction, 6–7 points to high addiction and 8–10 points to very high addiction.[14]

IBM SPSS software package (v.22.0) was used for statistical analysis. Paired *t*-test was used for normally distributed values, and Wilcoxon signed-rank test for non-parametric data. The chi-square test was used for comparison of categorical data. Statistical significance was set at $p<0.05$.

The study was conducted with the approval of the Karabuk University Non-Interventional Clinical Studies Ethics Committee (Approval No: 2020/198, 27/02/2020).

RESULTS

Between January and December 2018, 457 people applied to the smoking cessation outpatient clinic of the Family Medicine Department, Training and Research Hospital, Karabuk University. Of these, 74 could not quit smoking, 98 did not come for follow-up and 46 had incomplete examinations. Hence, 239 individuals who met the study criteria were included. Of these, 55.2% (132) individuals were women. Their mean (SD) age was 41.7 (10.9) years, 66.1% of them were in the age group of 31–50 years, 54.9% were college graduates and 77% were working in a job. The alcohol use rate was 5% and 27.7% had comorbid conditions. The mean FTND score of the study group was 7.06 (2.0), and 47.7% of them were highly addicted. The mean number of cigarettes consumed was 18.1 (11.2) packs/year and 42.3% had been smoking for 11–20 years (Table I).

When the individuals' blood tests before and 6 months after quitting smoking were compared, a significant decrease was observed in their haemoglobin, haematocrit, mean corpuscular volume (MCV), white blood cells (WBC), red blood cells (RBC), neutrophil, platelet, MPV, RDW, platelet distribution width (PDW), total cholesterol, triglyceride, low-density lipoprotein (LDL) levels; and a significant increase in their HDL levels compared to those before quitting smoking. It was also observed that there was a statistically significant decrease in their NLR, PLR, MPVLR and MHR after cessation of smoking compared with before cessation (Table II).

We found a negative correlation between the cigarette pack/year and FTND addiction levels and the change in HDL after cessation of smoking. There was a positive correlation between the cigarette pack/year and FTND levels and the changes in haemogram values, other blood lipid parameters, NLR, PLR, MPVLR and MHR after smoking cessation (Table III).

DISCUSSION

We found that, after smoking cessation, there was a significant decrease in haemoglobin, haematocrit, MCV, WBC, neutrophil, platelet, MPV, RDW, PDW, cholesterol, triglyceride, LDL levels,

TABLE I. Demographic characteristics and smoking habits of participants

Variable	Participants, *n* (%)
Gender	
Women	132 (55.2)
Men	107 (44.8)
Mean (SD) age in years, (range)	41.7 (10.9); (18–61)
≤30	52 (21.7)
31–50	158 (66.1)
≥51	29 (12.2)
Working status	
Not working	79 (33.0)
Working	160 (77.0)
Education	
Primary school	108 (45.1)
High school	131 (54.9)
Alcohol use	
Yes	12 (5.0)
No	227 (95.0)
Mean (SD) cigarettes consumed (pack/year), (range)	18.1 (11.2), (1–55)
≤10	73 (30.5)
11–20	101 (42.3)
21–30	43 (17.9)
≥31	22 (9.3)
Mean (SD) Fagerstrom test for nicotine dependence	7.06 (2.0)
Very little	10 (4.2)
Little	19 (7.9)
Middle	24 (10.1)
High	72 (30.1)
Very high	114 (47.7)
Additional disease history	
No	173 (72.3)
Chronic lung disease	5 (2.1)
Diabetes mellitus	8 (3.3)
Cardiovascular diseases	25 (10.5)
Psychiatric illness	9 (3.7)
Others	19 (8.1)
Total	239 (100)

TABLE II. Comparison of complete blood counts, blood lipid levels, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, mean platelet volume/lymphocyte ratio and monocyte high density lipoprotein ratio values of the participants before and after cessation of smoking

Parameter	Mean (SD) values		p value
	Before cessation	6 months after cessation	
Haemoglobin (g/dl)	14.10 (1.75)	12.45 (1.64)	<0.001
Haematocrit (%)	41.89 (4.46)	39.91 (4.31)	<0.001
MCV (fl)	87.70 (6.25)	86.52 (5.21)	<0.001
WBC (10^3/mm^3)	9.94 (4.21)	7.15 (1.74)	<0.001
RBC (10^6/mm^3)	4.78 (0.47)	4.38 (0.59)	<0.001
Neutrophils (10^3/mm^3)	4.69 (1.60)	4.31 (1.30)	<0.001
Lymphocytes (10^3/mm^3)	2.65 (1.66)	2.42 (0.81)	0.53
Platelets (10^3/mm^3)	267.29 (65.21)	257.04 (58.71)	<0.001
MPV (fl)	10.03 (1.01)	9.81 (1.31)	0.001
RDW (%)	13.98 (2.00)	13.49 (1.39)	<0.001
PDW (fl)	14.48 (2.51)	14.31 (2.52)	<0.001
Monocytes (10^3/mm^3)	0.50 (0.42)	0.46 (0.18)	0.06
Eosinophils (10^3/mm^3)	0.18 (0.14)	0.58 (0.4)	0.17
Basophils (10^3/mm^3)	0.042 (0.025)	0.043 (0.024)	<0.001
HDL (mg/dl)	50.26 (12.26)	55.10 (12.41)	<0.001
Cholesterol (mg/dl)	194.55 (39.76)	189.32 (38.39)	<0.001
Triglyceride (mg/dl)	176.64 (102.19)	159.24 (81.53)	<0.001
LDL (mg/dl)	110.68 (33.48)	103.21 (23.75)	<0.001
NLR	2.35 (1.58)	1.94 (0.95)	0.01
PLR	127.88 (60.88)	115.66 (46.38)	<0.001
MPVLR	4.92 (2.52)	4.45 (1.59)	0.001
MHR	0.01 (0.008)	0.008 (0.004)	<0.001

MCV mean corpuscular volume WBC white blood cells RBC red blood cells MPV mean platelet volume MPVLR MPV lymphocyte ratio RDW red cell distribution width PDW platelet distribution width HDL high-density lipoprotein MHR monocyte HDL ratio LDL low-density lipoprotein NLR neutrophil/lymphocyte ratio PLR platelet/lymphocyte ratio

TABLE III. Correlation analysis between the change in blood parameters of those who quit smoking and the pack/year and Fagerstrom addiction level

Parameter	Pack/year		Fagerstrom	
	r^1	p^1	r^2	p^2
Haemoglobin (g/dl)	0.639	<0.001	0.643	<0.001
Haematocrit (%)	0.813	<0.001	0.827	<0.001
MCV (fl)	0.902	<0.001	0.913	<0.001
MPV (fl)	0.671	<0.001	0.671	<0.001
RDW (%)	0.733	<0.001	0.743	<0.001
HDL (mg/dl)	–0.906	<0.001	–0.914	<0.001
Cholesterol (mg/dl)	0.897	<0.001	0.897	<0.001
Triglyceride (mg/dl)	0.910	<0.001	0.911	<0.001
LDL (mg/dl)	0.834	<0.001	0.836	<0.001
NLR	0.275	<0.001	0.276	<0.001
PLR	0.576	<0.001	0.576	<0.001
MPVLR	0.535	<0.001	0.530	<0.001
MHR	0.382	<0.001	0.402	<0.001

p value, Pearson partial correlation test *r* correlation coefficient
MCV mean corpuscular volume MPV mean platelet volume
MPVLR MPV lymphocyte ratio RDW red cell distribution width
HDL high-density lipoprotein MHR monocyte HDL ratio
LDL low-density lipoprotein NLR neutrophil/lymphocyte ratio
PLR platelet/lymphocyte ratio

NLR, PLR, MPVLR, and MHR, and a significant increase in HDL levels. We also observed that the amount of smoking and the level of dependence were negatively correlated with HDL, and positively correlated with haemogram values, other blood lipid parameters, NLR, PLR, MPVLR and MHR.

Cigarette smoke contains more than 4000 toxic agents that have negative effects on human health. The carbon monoxide formed by smoking causes a decrease in the oxygen-carrying capacity of haemoglobin by binding to haemoglobin faster than oxygen, and this leads to impaired oxygenation of tissues and changes in haematological parameters. Hence, haemoglobin levels increase to compensate for the reduced oxygen-carrying capacity in smokers.[15] Free radicals and peroxides from cigarette smoke affect the synthesis of prostaglandins and thromboxane and play a role in the pathogenesis of various diseases, including atherosclerosis, carcinoma and inflammatory processes.[16] Fricker *et al*. reported that cigarette consumption reduced tissue oxygen supply and caused systemic hypoxia.[17] Malenica *et al*. reported that haemoglobin and MCV levels were significantly higher in smokers compared to non-smokers, but there was no difference in RDW level.[4] While Alkhedaide reported that smoking caused a significant increase in RBC, haemoglobin and haematocrit levels,[18] Whitehead *et al*. found a significant increase in haemoglobin, RDW, haematocrit and neutrophil values in smokers compared to non-smokers.[19] Similarly, in our study, a significant decrease was found in the individuals' haemoglobin, haematocrit, MCV, RBC and RDW levels 6 months after cessation of smoking.

We found that there were significant changes in WBC levels after quitting smoking. It is known that the leucocyte and neutrophil counts are also higher in smokers and it has been assumed that the atherogenic effect of smoking may be partially mediated by leucocytes.[4] The total leukocyte count encompasses several cell types such as granulocytes, lymphocytes and monocytes, all of which potentially play a different role. While lymphocytes represent a more favourable immune response, neutrophils cause a destructive inflammatory reaction. NLR, a composite marker derived from the use of absolute neutrophil and lymphocyte counts, is a well-studied marker for survival in patients with cancer and cardiovascular diseases.[20,21] Aula and Qadir showed that there was a significant increase in the smokers' leucocyte, neutrophil, eosinophil, basophil, lymphocyte and monocyte levels compared to non-smokers.[22] In a similar study by Kumar *et al*., a significant increase in neutrophil and eosinophil counts was reported in smokers.[23] We found that, 6 months after cessation of smoking, neutrophil and lymphocyte levels and consequently the NLR decreased significantly. Fest *et al*. found that NLRs were higher in smokers, elderly patients and those with a history of diabetes, cancer or cardiovascular disease. However, they reported that smoking was an important confounder and after adjustment for this factor, only a part of the association between NLR and mortality was explained by smoking.[5]

Among the markers of inflammation involved in atherosclerosis, increasing importance has been given to circulating blood components such as subtype leucocyte and platelet counts, and future cardiovascular events in healthy subjects.[5,7,24] Similar to NLR, PLR is also increasingly being referred in clinical cardiovascular practice as a marker of inflammation, since these ratios can reflect an acute episode of inflammation and acute physiological stress.[24–26] In a study on secondary polycythaemia and leucocytosis in smokers, it was emphasized that tobacco smoking could cause inflammatory conditions in both alveolar tissues or a vascular damage that

leads to an immune response demonstrated by leucocytosis and lymphopoiesis.[18] According to recent studies, PLR is seen as a determinant of mortality in heart, lung diseases and some oncological diseases, while studies on atherosclerotic coronary artery disease, which is accepted as a chronic subclinical systemic inflammatory disease, reveal a significant relationship between cardiovascular risk and NLR and PLR.[6] It was also reported that increased platelet activation plays an important role in the initiation and progression of atherosclerosis.[27] High MPV, indicating platelet activation, indicates large platelets. Large platelets have more granules and higher thromboxane A2 levels, and aggregate faster with collagen.[25] Since large platelets are more active metabolically and enzymatically, platelet diameter reflects platelet activity better than platelet number.[28,29] Braekkan *et al*. reported that the platelet count had no effect on the risk of deep vein thrombosis, but the risk increased with high MPV levels, and that identification of MPV as a risk factor for deep-vein thrombosis suggested that platelet size may be a common risk factor for both arterial and venous thrombosis.[26] There are many studies showing that chronic smoking causes platelet activation.[30,31] Gumus *et al*. reported that, in the smoker group, they found an increase in the NLR, a decrease in the PLR, and an increase in the MPV/platelets ratio which indicates risk of thromboembolism.[3] Tulgar *et al*. found that NLR and PLR were significantly higher in smokers, but there was no difference in the MPV level.[32] Many studies have reported increased MPV levels especially in coronary artery patients and asserted that high MPV levels are an independent risk factor for myocardial infarction and stroke.[11,12,26] We found that the levels of platelets, PLR and MPV significantly decreased after cessation of smoking. Varol *et al*. reported that MPV levels were higher in smokers compared to non-smokers, and the MPV levels of those who quit smoking during the study period decreased significantly compared to the basal levels 3 months after quitting.[25]

MPVLR has been proposed as a new biomarker for inflammatory responses and thrombosis.[28] As mentioned above, large platelets are active metabolically and enzymatically. The larger-sized platelets do not only accelerate the formation of coronary artery thrombosis but also exacerbate the inflammatory response of the body.[33] A lymphocyte is one of the earliest cells involved in the formation of atherosclerotic plaque, and the reduction of lymphocytes contributes to the growth and rupture of the plaque and expansion of the infarcted area.[23] Hudzik *et al*.[34] found that patients with elevated MPVLR had worse angiographic features, which may indicate a greater thrombus burden. They concluded that elevated MPVLR was an independent risk factor of early and late mortality following ST-segment elevation myocardial infarction. Chen *et al*. found a significant negative correlation between MPVLR and NLR levels and left ventricular ejection fraction.[35] Sahinli *et al*. found that both disease-free and overall survival of patients with elevated MPVLR were worse than those with low MPVLR.[36] We found that MPVLR levels, which were reported to be a negative inflammatory marker, especially in cardiovascular and some malignant diseases, significantly decreased after cessation of smoking.[9,10] These results support the effect of smoking on inflammation, oxidative stress and alterations of antithrombotic and fibrinolysis systems.

Inflammation and oxidative stress are well-known mechanisms in the development and progression of atherosclerosis. Monocytes and macrophages play a key role in the development and progression of atherosclerosis. Following endothelial dysfunction, monocytes adhere to the endothelium tightly and migrate into the subendothelial layer. They then maturate into macrophages that ingest oxidized LDL cholesterol and form dangerous foam cells. Foam cells secrete pro-inflammatory cytokines that induce the local inflammatory response around the atherosclerotic lesion.[12,37] Contrarily, HDL molecules counteract the migration of macrophages and promote efflux of oxidized cholesterol from these cells.[37] There is also an interaction between HDL cholesterol and monocytes, which limits the inflammatory response that occurs while monocytes differentiate into macrophages.[12] Therefore, monocytes show a pro-inflammatory effect, but HDL cholesterol functions as a reversal factor during this process. MHR, the ratio of monocyte count to the HDL cholesterol level, was defined to be an easy calculable cardiovascular prognostic marker indicating the extent of the inflammation and oxidative stress.[38] Cigarette smoking is an important and independent risk factor for atherosclerosis, coronary artery disease, peripheral vascular disorders, etc. and several studies provide evidence that tobacco is strongly associated with altering the normal status of the lipid profile.[39,40] In addition, many studies have shown that smoking is associated with systemic inflammatory response and vascular endothelial damage.[13,41,42] Anandha Lakshmi *et al*. reported higher levels of total cholesterol, triglyceride, LDL and VLDL; but lower HDL levels in smokers compared to non-smokers.[1] Ito *et al*. reported low levels of HDL in smokers.[43] Y1 lmaz and Kayançiçek, found negative changes in blood lipid parameters and increased MHRs in smokers, and they asserted that MHR may be used as a surrogate marker of inflammation and endothelial dysfunction in smokers.[38] In our study, 6 months after quitting smoking, a significant decrease was found in total cholesterol, triglyceride, LDL levels and MHRs, and a significant increase in HDL levels. These results are consistent with the results of similar studies and may show that the inflammatory and atherosclerotic effects improve upon quitting smoking.

In our study, high levels of cigarette pack/year and FTND were positively correlated with changes in haemogram values, blood lipid parameters, NLR, PLR, MPVLR and MHR after smoking cessation. Anandha Lakshmi *et al*.[1] found haematocrit and haemoglobin levels to be significantly higher in smokers, and among smokers the RBC count was found to significantly increase as the intensity of smoking increased. Similarly, in the study by Y1 lmaz and Kayançiçek, a positive correlation was found between plasma lipid parameters and MHRs and cigarette pack/year.[38] These results show that the more the cigarettes consumed, the greater the negative effects due to smoking.

The limitation of our study is that it is a single-centre and retrospective study. As this is a self-controlled and retrospective clinical trial, the results were not compared with age- and gender-matched non-smoking normal controls and the clinical implications of observations and potential for intervention has not been assessed. The strength of our study lies in that we studied the changes in NLR, PLR, MPVLR and MHR together after quitting smoking.

Conclusion

We observed that, after quitting smoking, haemoglobin, haematocrit, MCV, WBC, neutrophil, platelet, MPV, RDW, PDW, cholesterol, triglyceride and LDL levels, and NLR, PLR, MPVLR and MHR decreased; and HDL levels increased. These effects were found to correlate with the intensity of smoking and the level of addiction. Based on our results, inflammation,

atherosclerosis and thrombotic effects caused by smoking and associated with many diseases, especially cardiovascular diseases, regress with cessation of smoking. Hence, determining the blood cell levels and the ratios of cells to each other by a simple examination such as haemogram can be a guide in the evaluation of these effects.

Conflicts of interest. None declared

REFERENCES

1 Anandha Lakshmi S, Anandhi Lakshmanan GK, Saravanan A. Effect of intensity of cigarette smoking on haematological and lipid parameters. *J Clin Diagn Res* 2014;**8:**BC11–BC13.
2 Gossett LK, Johnson HM, Piper ME, Fiore MC, Baker TB, Stein JH. Smoking intensity and lipoprotein abnormalities in active smokers. *J Clin Lipidol* 2009; **3:**372–8.
3 Gumus F, Solak I, Eryilmaz MA. The effects of smoking on neutrophil/lymphocyte, platelet//lymphocyte ratios. *Bratisl Lek Listy* 2018;**119:**116–19.
4 Malenica M, Prnjavorac B, Bego T, Dujic T, Semiz S, Skrbo S, *et al*. Effect of cigarette smoking on haematological parameters in healthy population. *Med Arch* 2017;**71:**132–6.
5 Fest J, Ruiter TR, Groot Koerkamp B, Rizopoulos D, Ikram MA, van Eijck CH, *et al*. The neutrophil-to-lymphocyte ratio is associated with mortality in the general population: The Rotterdam study. *Eur J Epidemiol* 2019;**34:**463–70.
6 Kim DS, Shin D, Lee MS, Kim HJ, Kim DY, Kim SM, *et al*. Assessments of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in Korean patients with psoriasis vulgaris and psoriatic arthritis. *J Dermatol* 2016;**43:**305–10.
7 Akboga MK, Canpolat U, Yayla C, Ozcan F, Ozeke O, Topaloglu S, *et al*. Association of platelet to lymphocyte ratio with inflammation and severity of coronary atherosclerosis in patients with stable coronary artery disease. *Angiology* 2016;**67:**89–95.
8 Gulcan M, Varol E, Etli M, Aksoy F, Kayan M. Mean platelet volume is increased in patients with deep vein thrombosis. *Clin Appl Thromb Hemost* 2012;**18:** 427–30.
9 Kilincalp S, Coban S, Akinci H, Hamamc1 M, Karaahmet F, Coskun Y, *et al*. Neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and mean platelet volume as potential biomarkers for early detection and monitoring of colorectal adenocarcinoma. *Eur J Cancer Prev* 2015;24:328–33.
10 Kose N, Akin F, Yildirim T, Ergun G, Altun I. The association between the lymphocyte-to-monocyte ratio and coronary artery disease severity in patients with stable coronary artery disease. *Eur Rev Med Pharmacol Sci* 2019;**23:** 2570–5.
11 Azab B, Torbey E, Hatoum H, Singh J, Khoueiry G, Bachir R, *et al*. Usefulness of red cell distribution width in predicting all-cause long-term mortality after non-ST-elevation myocardial infarction. *Cardiology* 2011;**119:**72–80.
12 Canpolat U, Çetin EH, Cetin S, Aydin S, Akboga MK, Yayla C, *et al*. Association of monocyte-to-HDL cholesterol ratio with slow coronary flow is linked to systemic inflammation. *Clin Appl Thromb Hemost* 2016;**22:**476–82.
13 Li H, Srinivasan SR, Chen W, Xu JH, Li S, Berenson GS. Vascular abnormalities in asymptomatic, healthy young adult smokers without other major cardiovascular risk factors: The Bogalusa Heart Study. *Am J Hypertens* 2005;**18:**319–24.
14 Svicher A, Cosci F, Giannini M, Pistelli F, Fagerström K. Item response theory analysis of Fagerström test for cigarette dependence. *Addict Behav* 2018;**77:** 38–46.
15 Aitchison R, Russell N. Smoking—A major cause of polycythaemia. *J R Soc Med* 1988;**81:**89–91.
16 Tirlapur VG, Gicheru K, Charalambous BM, Evans PJ, Mir MA. Packed cell volume, haemoglobin, and oxygen saturation changes in healthy smokers and non-smokers. *Thorax* 1983;**38:**785–7.
17 Fricker M, Goggins BJ, Mateer S, Jones B, Kim RY, Gellatly SL, *et al*. Chronic cigarette smoke exposure induces systemic hypoxia that drives intestinal dysfunction. *JCI Insight* 2018;**3:**94040.
18 Alkhedaide AQ. Tobacco smoking causes secondary polycythemia and a mild leukocytosis among heavy smokers in Taif City in Saudi Arabia. *Saudi J Biol Sci* 2020;**27:**407–11.
19 Whitehead TP, Robinson D, Allaway SL, Hale AC. The effects of cigarette smoking and alcohol consumption on blood haemoglobin, erythrocytes and leucocytes: A dose related study on male subjects. *Clin Lab Haematol* 1995;**17:**131–8.
20 Horne BD, Anderson JL, John JM, Weaver A, Bair TL, Jensen KR, *et al*. Which white blood cell subtypes predict increased cardiovascular risk? *J Am Coll Cardiol* 2005;**45:**1638–43.
21 Templeton AJ, McNamara MG, Šeruga B, Vera-Badillo FE, Aneja P, Ocaña A, *et al*. Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: A systematic review and meta-analysis. *J Natl Cancer Inst* 2014;**106:**dju124.
22 Aula FA, Qadir FA. Effects of cigarette smoking on some immunological and hematological parameters in male smokers in Erbil city. *J Natl Cancer Inst* 2013; **147:**1–8.
23 Kumar J, Kumar G, Sharma A, Ahmad Khan F, Sharma S. The effect of smoking on the blood parameters of young adults. *J Clin Diagn Res* 2012;**6:**1244–7.
24 Serrano CV Jr., de Mattos FR, Pitta FG, Nomura CH, de Lemos J, Ramires JA, *et al*. Association between neutrophil-lymphocyte and platelet-lymphocyte ratios and coronary artery calcification score among asymptomatic patients: Data from a cross-sectional study. *Mediators Inflamm* 2019;**2019:**6513847.
25 Varol E, Icli A, Kocyigit S, Erdogan D, Ozaydin M, Dogan A. Effect of smoking cessation on mean platelet volume. *Clin Appl Thromb Hemost* 2013;**19:**315–19.
26 Braekkan SK, Mathiesen EB, Njølstad I, Wilsgaard T, Størmer J, Hansen JB. Mean platelet volume is a risk factor for venous thromboembolism: The Tromsø study, Tromsø, Norway. *J Thromb Haemost* 2010;**8:**157–62.
27 Collet JP, Kerneis M, Hulot JS, O'Connor SA, Silvain J, Mansencal N, *et al*. Point-of-care genetic profiling and/or platelet function testing in acute coronary syndrome. *Thromb Haemost* 2016;**115:**382–91.
28 Kurtul A, Acikgoz SK. Usefulness of mean platelet volume-to-lymphocyte ratio for predicting angiographic no-reflow and short-term prognosis after primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction. *Am J Cardiol* 2017;**120:**534–41.
29 Thompson CB, Eaton KA, Princiotta SM, Rushin CA, Valeri CR. Size dependent platelet subpopulations: Relationship of platelet volume to ultrastructure, enzymatic activity, and function. *Br J Haematol* 1982;**50:**509–19.
30 Takajo Y, Ikeda H, Haramaki N, Murohara T, Imaizumi T. Augmented oxidative stress of platelets in chronic smokers. Mechanisms of impaired platelet-derived nitric oxide bioactivity and augmented platelet aggregability. *J Am Coll Cardiol* 2001;**38:**1320–7.
31 Lupia E, Bosco O, Goffi A, Poletto C, Locatelli S, Spatola T, *et al*. Thrombopoietin contributes to enhanced platelet activation in cigarette smokers. *Atherosclerosis* 2010;**210:**314–19.
32 Tulgar YK, Cakar S, Tulgar S, Dalkilic O, Cakiroglu B, Uyanik BS. The effect of smoking on neutrophil/lymphocyte and platelet/lymphocyte ratio and platelet 1ndices: A retrospective study. *Eur Rev Med Pharmacol Sci* 2016;**20:**3112–18.
33 Kiris T, Çelik A, Vari_ E, Akan E, Akyildiz ZI, Karaca M, *et al*. Association of lymphocyte-to-monocyte ratio with the mortality in patients with ST-elevation myocardial infarction who underwent primary percutaneous coronary intervention. *Angiology* 2017;**68:**707–15.
34 Hudzik B, SzkodziD ski J, Lekston A, Gierlotka M, PoloD ski L, G sior M. Mean platelet volume-to-lymphocyte ratio: A novel marker of poor short- and long-term prognosis in patients with diabetes mellitus and acute myocardial infarction. *J Diabetes Complications* 2016;**30:**1097–102.
35 Chen X, Meng Y, Shao M, Zhang T, Han L, Zhang W, *et al*. Prognostic value of pre-infarction angina combined with mean platelet volume to lymphocyte count ratio for no-reflow and short-term mortality in patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention. *Med Sci Monit* 2020;**26:**e919300.
36 Sahinli H, Turker S, Eren T, Cilbir E, Altinbas M. The mean platelet volume to lymphocyte ratio: A new prognostic marker in resected gastric cancer. *Eur J Med Invest* 2020;**4:**155–60.
37 Kirişçi M. A promising marker for carotid artery disease: Monocyte to high-density lipoprotein ratio (MHR). *Sakarya Med J* 2020;**10:**93–8.
38 Yilmaz M, Kayançiçek H. A new inflammatory marker: Elevated monocyte to HDL cholesterol ratio associated with smoking. *J Clin Med* 2018;**7:**E76.
39 Guedes DP, Guedes JE, Barbosa DS, de Oliveira JA. Uso de tabaco e perfil lipídico-lipoprotéico plasmático em adolescents [Tobacco use and plasma lipid-lipoprotein profile in adolescents]. *Rev Assoc Med Bras* 2007;**53:**59–63.
40 Aggarwal A, Aggarwal S, Sarkar PG, Sharma V. Predisposing factors to premature coronary artery disease in young (age <45 years) smokers: A single center retrospective case control study from India. *J Cardiovasc Thorac Res* 2014;**6:** 15–19.
41 Luo HL, Zang WJ, Lu J, Yu XJ, Lin YX, Cao YX. The protective effect of captopril on nicotine-induced endothelial dysfunction in rat. *Basic Clin Pharmacol Toxicol* 2006;**99:**237–45.
42 Heeschen C, Weis M, Cooke JP. Nicotine promotes arteriogenesis. *J Am Coll Cardiol* 2003;**41:**489–96.
43 Ito T, Nishiwaki M, Ishikawa T, Nakamura H. CETP and LCAT activities are unrelated to smoking and moderate alcohol consumption in healthy normolipidemic men. *Jpn Circ J* 1995;**59:**541–6.