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Original Article

Impact of chronic cigarette smoking on blood count indices, erythrocyte sedimentation rate and C-reactive protein as inflammatory markers in healthy individuals

Pulmonology

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ABSTRACT

Background: Cigarette smoking is awell-known significant contributor to the development of many illnesses that having an inflammatory component. Smoking has both acute and chronic effects on haematological parameters.

Objective: to assess the impact of cigarette smoking on complete blood count (CBC) indices and some inflammatory markers erythrocytic sedemitation rate (ESR) and C-reactive protein(CRP).

Methodology: this case-control study was conducted on 30 healthy active smokers and 30 healthy passive smokers and 30 age and sex-matched healthy non-smokers subjects. Data regarding age, sex, smoking index, and smoking duration were recorded. CBC, differential leucocytic count, platelets/lymphocytes ratio (PLR), neutrophils/lymphocytes ratio (NLR), CRP and ESR were measured.

Results: A statistically significant differences were identified between active and passive smokers groups regarding CBC and inflammatory markers parameters except for neutrophil %. ESR and CRP had no statistically significant difference. Statistically, significant differences have been identified between active smokers group and control group regarding all CBC indices and inflammatory markers e.g PLR, NLR, ESR and CRP, while no statistical difference has been identified between passive smokers group and control group regarding CBC and inflammatory markers parameters except monocyte % and ESR, which had statistically significant difference.

Conclusion: Passive smoking affects hematological indices and inflammatory markers as well as active smoking. Accordingy, it is important to keep in mind that cigarette smoking either active or passive is one of differential diagnoses of change in blood indices.

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Keywords: Smoking, complete blood count, active smoking, passive smoking, smoking effects.

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INTRODUCTION

There is no level of tobacco exposure that is safe; all kinds of tobacco are detrimental. The most common form of tobacco use in the world is cigarette smoking [1]. Smoke from cigarettes contains toxic ingredients that circulate throughout the body and harm it in many ways. These ingredients in the form of gases, vapors, and particles e.g. carbon monoxide (CO), ammonia, pyrene, hydrogen cyanide, phenols, formaldehyde, benzene, nitrosamines, nicotine, tar, burning tobacco and paper yields more than 4,000 chemical compounds. Nicotine and CO are two of the substances that are thought to be most accountable for pharmacological effects among free radicals [2].

Secondhand smoking (SHS) (passive smoking) poses a huge public health issue, and researchers are increasingly concerned about the potentially hazardous impacts of SHS. It has been revealed that there is a connection between SHS and particular illnesses, including lung cancer and cardiovascular illnesses. While its relation to other health problems is still under research [3]. Evidence gathered over the last four decades has consistently shown that smoking tobacco, whether actively or passively, increases morbidity and the chance of premature mortality, as well as having detrimental short- and long-term impacts on human body system [4].

Many studies showed that smoking had a negative impact on human health and was a risk factor for developing a number of pathological conditions and diseases, including metabolic syndrome, pancreatitis, gastro-intestinal diseases, chronic obstructive pulmonary

disease, cancer, and some autoimmune disorders[5]. Although the precise mechanisms of such problems in smokers are unknown, it is assumed that anomalies in blood morphology, infections, inflammation, oxidative stress, and changes to the antithrombotic and fibrinolytic systems are to blame [5]

The complete blood count (CBC) is used to compute the neutrophil/lymphocyte ratio NLR and platelet/ lymphocyte ratio (PLR), which are affordable and easily accessible. The NLR and PLR together may be employed as markers of inflammation and as prognostic indicators for systemic illnesses. PLR provides information on the aggregation and inflammatory pathways, and it might be more useful in predicting the burden of coronary atherosclerosis than platelet or lymphocyte count alone[6].

Even though the majority of the effects of smoking are reversed following quitting, certain inflammatory mediators, such as CRP, are still significantly elevated in former smokers up to 10–20 years following quitting, indicating that low-grade inflammatory responses are still present in those who have quit smoking[7]. This work was carried out to assess the impact of cigarette smoking on CBC indices and some inflammatory markers e.g. erythrocytic sedemitation rate (ESR) and CRP.

SUBJECTS AND METHODS

This case-control study has been performed at Chest diseases department, Al-Zahra university hospital, Al-Azhar University, Cairo, Egypt. It was conducted from June 2021 to December 2021.The study was conducted on 90 subjects, they were classified into:

1. **Asymptomatic active cigarette smokers:** included 30 asymptomatic current cigarette smokers, who has smoked 100 cigarettes throughout his life[8].Based on their smoking index (cigarette/ year), they were classified into 3 subgroups; mild active cigarette smokers (<400 cigarette/ year), moderate active cigarette smokers (400-800 cigarette /year), and heavy active cigarette smokers (≥ 800 cigarette /year) [9].
2. **Asymptomatic passive cigarette smokers:** included 30 asymptomatic passive smokers, who are smoking a mixture of secondhand smoke (which is the smoke that comes from a cigarette's burning tip or another smoked tobacco product)[10].
3. **Control group (non-smokers group):** included 30 age and sex matched healthy who is either life-long non-smoker or smoke of no more than 100 cigarettes in his lifetime and not currently smoke[11].

Exclusion criteria

Patients known to have any chest diseases, infections, liver or kidney diseases, blood diseases, malignant, autoimmune diseases, diabetes mellitus, hypertension, hypo/hyperthyroidism, metabolic syndrome, and hematological abnormalities were excluded from the study. Pregnant women and those receiving any medical treatment, or alcohol as well as those who smoke other forms of smoking were not included into the study.

The participants were given an explanation of the study's goals and methods. This study was approved by the institutional review board of faculty of medicine for girls, Al-Azhar University's, Cairo, Egypt. Each participant in the study provided their informed consent prior to enrollment, and participation was completely voluntary. Each participant had the right to decline participation or leave the research at any moment without giving a reason or affecting their rights of medical care. Additionally, the data were coded and made anonymous to guarantee participant confidentiality.

Methods

A thorough history was taken with special emphasis on age/yrs., sex, age of starting smoking/yrs., number of cigarettes smoked each day, and smoking duration/yrs. The smoking index (pack/year) has been calculating by multiplying the number of packs smoked per day by the number of years of smoking. Liver function tests, kidney function tests, CBC, and fasting blood sugar were done using HITACH9-911 TM autoanalyzer to exclude participates with chronic diseases that could affect the CBC indices and inflammatory mediators.

Venous blood sample was obtained using minimal tourniquet pressure as platelets are fragile and are easily activated. The blood samples are immediately putted in ethylene diaminetetraacetic acid- containing tubes (Becton Dickinson Vacuum). Before processing, the sample was gently mixed and kept at room temperature. Hematological measurements were made within 1-2 hours of the blood sampling (Sysmex XE-21N, Kobe, Japan). Using a standard, commercially accessible calibrator kit, the analyzer has been calibrated every day. The following measurements, hematocrit (HCT), red blood corpuscle (RBC) count, RBCs indices e.g. mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), WBCs and platelets (PLTs)NLR and PLR were calculated as following: NLR = (absolute neutrophil count, cells/µL) / (absolute lymphocyte count, cells/µL).PLR = (platelet count,10^3/ul) / (absolute lymphocyte count, cells/µL).

Two milliliters of blood have been evacuated into a plain tube and allowed to clot for 20 minutes at room temperature prior to centrifugation at 3000 rpm for 20 minutes to determine the blood CRP level. The CRP level was measured by turbidimetric method (BioSystems, lot 19420). Two ml of the venous blood were evacuated into a tube containing 0.5 ml of sodium citrate for measurement of ESR using the Westergren method.

Statistical analysis

Version 24 of the Statistical Program for Social Science (SPSS) has been employed to analyze the data. For

parametric data, quantitative data has been presented as standard deviation (SD) and for non-parametric data as median with interquartile range (IQR). Frequency and percentage were employed to express qualitative data. When comparing two means, the independent-samples t-test was applied for significance (for data that is normally distributed). The Mann-Whitney U test has been utilized to compare two medians (for data that is abnormally distributed). Chi-square test was used for comparison of qualitative data. When comparing more than two means, a one-way analysis of variance (ANOVA) has been employed. When comparing more than two medians, Kruskal Wallis has been employed. The correlation among the relevant quantitative variables has been examined using Pearson's correlation coefficient (r). The correlation coefficient (r) value and the p value both helped to determine the direction and the intensity of the correlation. P-values of <0.05 have been deemed significant (95% confidence interval).

RESULTS

With regard to age and sex, there were no statistically significant differences between the studied groups. The mean ± SD of smoking index in active smokers' group was 193.5 ± 194.1, with 11 (36.7%) subjects were mild smokers, 10 subjects(33.3%) were moderate smokers, and 9 (30.0%) subjects were heavy smokers (table 1).

Table (2) shows that there were statistically significant increases of Hb, HCT, MCV, MCH, RBC, monocytes %, TLC, and neutrophils %, with statistically significant drop of lymphocyte % in the active smokers' group compared to either the passive smokers' group or the non-smokers' group. Significantly higher monocyte % in passive smokers group compared to non-smokers group. Additionally, there was a statistically significant increase in NLR among active smokers' group when compared to both passive smokers and non-smokers groups. When compared to non-smokers, both active and passive smokers had statistically significant increases in CRP. However, no significant difference in PLR and ESR was detected across the three groups studied.

Table (3) shows that heavy smokers had a statistically significant increase in of Hb, PLTs, and neutrophils (abs) in comparison to both moderate and mild smokers' groups, and in moderate smokers group in comparison to mild smokers group. However, no statistically significant change was found in HCT, RBCs count and RBCs indices between heavy, moderate, and mild smokers. Moreover, there was no statistically significant difference in inflammatory markers; NLR. PLR. CRP and ESR among mild, moderate, and heavy smokers' groups (p > 0.05).

Table (4) and figures (1 and 2) show that in the active smokers' group, the smoking duration was positively correlated with PLTs, neutrophils (abs) count, and NLR, while it was negatively correlated with lymphocytes %. Additionally, in the passive smoking group, the smoking duration was positively associated with NLR and negatively associated with lymphocyte (abs) count and lymphocytes%.

Table (1): Demographic data among the studied groups

Items		Active smokers (n = 30)	Passive smokers (n = 30)	Non-smoker's (n = 30)	Stat. test	P-value
Age (years)	Mean ±SD	38.5 ± 7.5	37.3 ± 9.9	33.8 ± 7.6	F = 2.43	0.09
Sex	Male	26 (86.7%)	22 (73.3%)	19 (63.6%)	X^2 = 0.3	0.23
	Female	4 (13.3%)	8 (26.7%)	11 (36.7%)		
Smoking duration		14.6 ± 6.7	16.8 ± 9.2			
Smoking index		193.5±194.1				
Smoking degree:						
Mild smokers: no. (%)		11 (36.7%)				
Moderate smokers: no. (%)		10 (33.3%)				
Heavy smokers: no. (%)		9 (30%)				

X^2: Chi-square test. F: F value of ANOVA.

Table (2): Comparison of complete blood count indices, neutrophil / lymphocyte ration, erythrocytic sedimentation rate, C-reactive protein, and platelet / lymphocyte ratio between the studied groups

CBC-indices		Active smokers (n = 30)	Passive smokers (n = 30)	Non-smokers (n = 30)	Stat. test and P value	MW
Hb g/dl	Median (IQR)	14(12.7- 14)	12(11- 13)	12(11- 13)	KW=17.2 p= 0.001*	P1:0.036* P2:0.005* P3:0.82
MCV fl/cell	Median (IQR)	87(83-89)	81(78-87)	81(78- 84)	KW=11.5 p= 0.003*	P1:0.01* P2:0.004* P3:0.74
MCH pg/cell	Median (IQR)	28(27-30)	26(25-28)	26(25-28)	KW=13.3 p= 0.001*	P1:0.035* P2:0.008* P3:0.56
MCHC g/dl	Median (IQR)	32(31-34)	32(30-33)	31(0-32)	KW=3.9 p= 0.137	
HCT %	Median (IQR)	43(39-47)	38(35-41)	37(35-40)	KW=18.7 p= 0.001*	P1:0.001* P2:0.001* P3:0.81
RBCs million/ul	Median (IQR)	5(4.7-5.2)	5(4-5)	5(4-5)	KW =6.3 p= 0.042*	P1:0.04* P2:0.01* P3:0.57
PLTs x10³/ul	Median (IQR)	229(177-290)	254(200-278)	234(189-260)	KW=1.89 p= 0.387	
TLC x10³/ul	Median (IQR)	8(6.8-8.3)	7(5.7-7	6(5-7.3)	KW=8.4 p= 0.015*	P1:0.017* P2:0.009* P3:0.815
Lymphocytes %	Median (IQR)	30(28-35)	35(29-41)	36(30-40)	KW=7.6 p= 0.022*	P1:0.018* P2:0.008* P3:0.759
Lymphocytes (abs)	Median (IQR)	2.4(2-2.9)	2.3(1.6-2.9	2.2(1.9-2.5)	KW=0.52 p= 0.769	
Monocytes %	Median (IQR)	8(6-9)	5(4-7)	6(5-8)	KW=18.6 p= 0.001*	P1:0.001* P2:0.045* P3:0.006
Eosinophils %	Median (IQR)	2 (2-3)	2 (1-3)	2 (1-3)	KW=1.77 p= 0.412	
Neutrophils %	Median (IQR	57(53-60)	54(49-58)	49(43-55)	KW=11.5 p= 0.003*	P1:0.455* P2:0.014* P3:0.08
Neutrophils (abs)	Median (IQR)	4.2(3-5.2)	3.3(3-4)	3(2.3-4.1)	KW=10.2 p= 0.006*	P1:0.01* P2:0.001* P3:0.35
NLR	Median (IQR)	1.85 (1.5-2.2)	1.6 (1.2-1.9)	1.4 (1-1.7)	KW=1.89 p= 0.022*	P1: 017* P2: 0.001* P3: 0.268
PLR	Median (IQR)	100 (72-132)	106 (88-129)	102 (76-119)	KW=1.4 p =0.49	
CRP (mg/L)	Median (IQR)	6 (5-8)	6 (4-7)	4 (2-6)	KW=7.55 p =0.023*	P1:0.219* P2: 0.005* P3: 0.099
ESR (mm/h)	Median (IQR)	10 (5-20)	11 (8-17)	11 (10-1)	KW=1.4 p= 0.49	

Hb: Hemoglobin, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, HCT: Haematocrit, RBC: Red blood corpuscle, PLT: Platelet, TLC: Total leucocytic count, NLR: neutrophil / lymphocyte ration, ESR: erythrocytic sedimentation rate, CRP: C-reactive

protein, PLR: platelet / lymphocyte ratio, KW: Kruskal Willis test., MW: Mann-Whitney test, P1: active smokers vs. passive smokers, P2: active smokers vs. non-smokers, P3: passive smokers vs. non-smokers, *: Significant p value (<0.05).

Table (3): Relation between smoking index (cigarette/year) and complete blood count indices, neutrophil / lymphocyte ration, erythrocytic sedimentation rate, C-reactive protein, and platelet / lymphocyte ratio among active smokers group

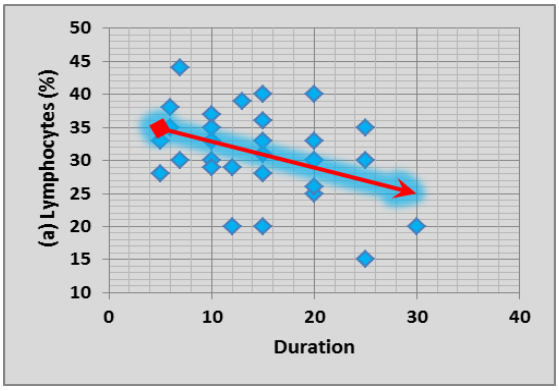
Items		Mild smokers (n = 11)	Moderate smokers (n = 10)	Heavy smokers (n = 9)	Stat. test and p value	MW
Hb (g/dl)	Median (IQR)	13(12-14)	13(12- 14)	14(14-15)	KW=9.08 p=0.011	P1: 0.048 P2: 0.041* P3: 0.038*
MCV (fl/cell)	Median (IQR)	87(85-88)	87(80-89)	88(82-90)	KW=0.68 p= 0.710	
MCH (pg/cell)	Median (IQR)	28(27-30)	29(26-30)	29(28-31)	KW=1.01 p= 0.602	
MCHC (g/dl)	Median (IQR)	32(31-34)	33(32-34)	31(31-32)	KW=5.2 p= 0.073	
HCT (%)	Median (IQR)	42(37-47)	43(37-44)	46(42-4)	KW=3.14 p= 0.208	
RBCs (million/ul)	Median (IQR)	5 (4-5	5(4-5)	5(5-6)	KW=5.58 p= 0.061	
PLTs (x10^3/ul)	Median (IQR)	170 (150-219)	214 (180-290)	300 (255-334)	KW=13.7 p= 0.001	P1: 0.029 P2: 0.001* P3: 0.021*
TLC (x10^3/ul)	Median (IQR)	7 (6-8)	7.5(6.5-8.3)	8(8-10)	KW=5.5 p= 0.06	
Lymphocytes (%)	Median (IQR)	33(30-37)	29(26 – 36)	30(25 – 34)	KW=1.47 P= 0.48	
Lymphocytes (abs)	Median (IQR)	2.3(1.8-2.9	2.5(1.7-2.9)	2.4(2-2.9)	KW=0.55 P= 0.75	
Monocytes (%)	Median (IQR)	8(6-8)	7(5-10)	9(7-10)	KW=1.27 p= 0.52	
Eosinophils (%)	Median (IQR)	2(2-3)	3(2-7)	2(2-3)	KW=2.6 p= 0.26	
Neutrophils (%)	Median (IQR)	53(50-59)	56(53-59)	59(55-66)	KW=5.04 p= 0.08	
Neutrophils (abs)	Median (IQR)	3.4(2.5-4.6)	4(2.7-4.7)	5.3(4.5-5.8)	KW=9.3 p= 0.009	P1: 0.061 P2: 0.003* P3: 0.042*
NLR	Median (IQR)	1.8 (1.4-2)	1.9 (1.5-2.3)	2 (1.7-2.7)	KW=3.02 p= 0.22	
PLR	Median (IQR)	72 (68-113)	102 (72-151)	114 (100-144)	KW=4.3, p= 0.11	
CRP (mg/L)	Median (IQR)	6 (5-8)	5 (4- 310)	8 (6-9)	KW=2.9, p= 0.23	
ESR (mm/h)	Median (IQR)	10 (5-20)	11 (8-17)	11 (10-18)	KW=1.4, p= 0.49	

Hb: Hemoglobin, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, HCT: Haematocrit, RBC: Red blood corpuscle, PLT: Platelet, TLC: Total leucocytic count, NLR: neutrophil / lymphocyte ration, ESR: erythrocytic sedimentation rate, CRP: C-reactive protein, PLR: Platelet / lymphocyte ratio, KW: Kruskal Willis test., MW: Mann-Whitney, P1: Mild smokers vs. moderate smokers, P2: Mild smokers vs. heavy smokers, P3: Moderate smokers vs. heavy smokers, *: Significant p value (<0.05).

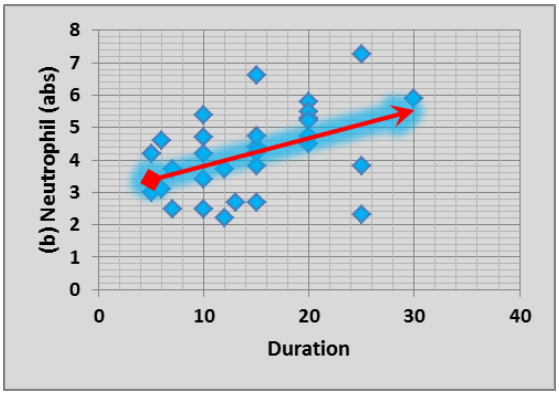
Table (4): Correlation of smoking duration with complete blood count indices in active and passive groups

Items	Active smokers' group		Passive smokers' group	
	r	p value	r	p value
Hb (g/dl)	0.27	0.155	-0.22	0.241
MCV (fl/cell)	0.13	0.486	0.17	0.375
MCH (pg/cell)	0.15	0.438	0.31	0.097
MCHC (g/dl)	-0.22	0.253	0.02	0.931
HCT %	0.35	0.059	-0.20	0.284
RBCs (million/ul)	0.34	0.066	-0.31	0.092
PLTs ($x10^3$/ul)	0.53	0.003*	-0.17	0.378
TLC ($x10^3$/ul)	0.30	0.113	-0.15	0.439
Lymphocytes (%)	-0.40	0.031*	-0.36	0.048*
Lymphocytes (Abs)	-0.05	0.811	-0.40	0.029*
Monocyte %	-0.04	0.817	-0.03	0.883
Eosinophil %	0.11	0.57	0.32	0.085
Neutrophil %	0.31	0.099	0.13	0.508
Neutrophil (Abs)	0.45	0.013*	-0.08	0.687
NLR	0.52	0.003*	0.40	0.03*
PLR	0.34	0.064	0.28	0.136
ESR (mg/l)	0.18	0.351	-0.27	0.142
CRP (mm/h)	0.09	0.624	-0.10	0.606

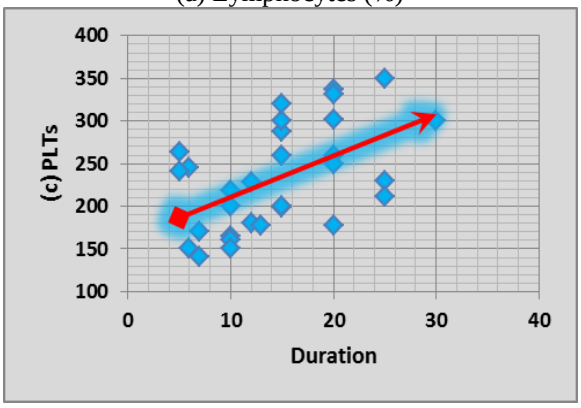
Hb: Hemoglobin, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, HCT: Haematocrit, RBC: Red blood corpuscle, PLT: platelet, TLC: Total leucocytic count, NLR: neutrophil / lymphocyte ration, ESR: erythrocytic sedimentation rate, CRP: C-reactive protein, PLR: platelet / lymphocyte ratio, r: correlation coefficient, NLR: neutrophil / lymphocyte ration, ESR: erythrocytic sedimentation rate, CRP: C-reactive protein, PLR: Platelet / lymphocyte ratio, *: Significant p value (<0.05).



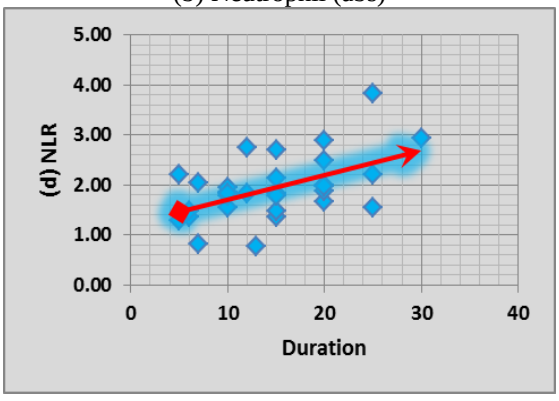
(a) Lymphocytes (%)



(b) Neutrophil (abs)

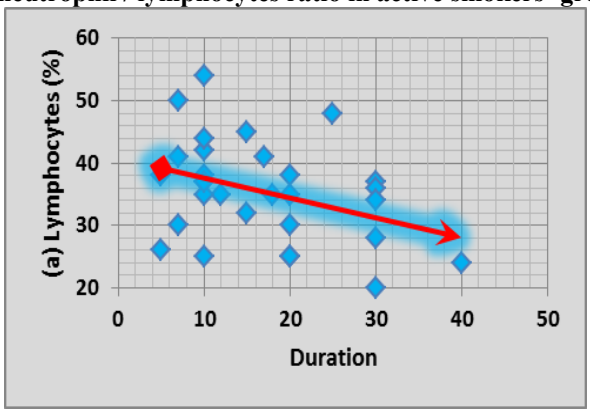


(c) PLTs

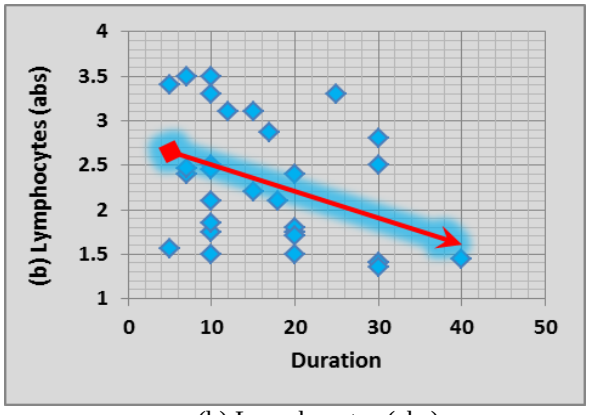


(d) NLR

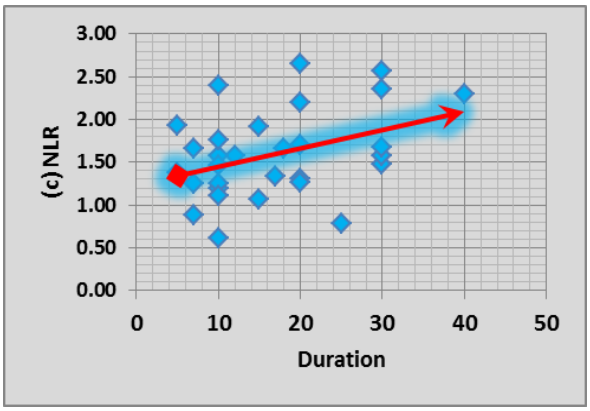
Figure (1): Correlation of smoking duration with lymphocytes %, neutrophil (abs) count, platelet and neutrophil / lymphocytes ratio in active smokers' group



(a) Lymphocytes (%)



(b) Lymphocytes (abs)



(b) NLR

Figure (2): Correlation of smoking duration with lymphocytes %, lymphocytes (abs) count and neutrophil / lymphocytes ratio in active smokers' group

DISCUSSION

The smoking-induced abnormalities in people who are classified as healthy smokers because they are asymptomatic with normal spirometry, radiography, and physical exams. In reality, "healthy smokers" are unhealthy[12]. Many studies focus on the pathophysiologic, immunologic, genetic, and structural changes that smoking has on healthy smokers' respiratory systems, including inflammation and pulmonary dysfunction. Several studies showed that smoking had negative health effects on humans and was a risk factor for developing a number of pathological disorders and diseases [13]. Therefore, the current study was conducted to assess the impact of active and passive cigarette smoking on CBC indices and some inflammatory markers e.g. ESR and CRP.

The Hb concentration are known to rise as a result of smoking, and CO exposure is thought to play a role in this. An inactive type of Hb with no ability to carry oxygen, carboxyhemoglobin, is produced when CO attaches to Hb. Additionally, carboxyhemoglobin causes a shift in the Hb dissociation curve to the left, which reduces Hb capacity to supply oxygen to tissues. Smokers continue to maintain a higher a Hb concentration than non-smokers in order to make up for the reduced oxygen-delivering ability [14]. Another explanation for tissue hypoxia is that high carboxyhemoglobin synthesis causes increased erythropoietin secretion, which in turn increases erythropoiesis. Smoking tobacco causes an increase in capillary permeability, which lowers plasma volume, mimicking the state of polycythemia, which is defined by an increasing proportion of RBCs in blood volume, which is also represented in increased hematocrit values[15]. The current study confirmed this explanation, as our findings showed that, while the HB, HCT, and RBCs indices were within the normal ranges there were highly statistically significant increases in Hb, HCT, and statistically significant increases in MCV, MCH (p 0.001), and RBCs count ($p \prec 0.05$) among active smokers in comparison to both passive and non- smokers groups. In terms of MCHC, there were no significant differences between the studied groups(table 2).Additionally, we find that among active smokers, heavy smokers subgroups show statistically significant increased Hb (p 0.011) while, the MCV, MCH, MCHC, HCT and RBCs were non-significantly differed between mild and moderate

smokers (table 3). These findings were consistent with the that of Muhammad et al. [16], who found significant rise of Hb, RBCs count, and MCH of different degrees in people who smoke in comparison to non-smokers of the same age groups, whereas the rise in MCV and MCHC values were found to be less marked and non-significant[16].Numerous investigations conducted at different times and locations are in line with our findings, with minor differences in all parameters. As Khalid et al. [17] and Maja et al. [13] demonstrated that smokers have a higher ratio of macrocytic RBCs and a lower red cell distribution width (RDW) in comparison to nonsmokers. Shah et al. [2] reported that smokers had greater Hb levels than nonsmokers, while Asif et al. [18]reported that smokers had higher MCV level and lower MCH and MCHC levels when compared to nonsmokers, but those studies didn't include the passive smokers. On the other hand, Andrease et al. [19] reported no difference between active, passive smokers or and control groups as regards RBCs parameters, but his study was done in symptomatic smokers.

Cigarette smokers are associated with high risk of arterial thrombosis. Platelet function disturbances, particularly aggregation, are thought to be the primary mechanism behind this pathology. Smoking's impact on platelet quantity, however, might also be a significant factor. It is still debatable whether smoking affects platelet counts[20]. In our study, there was non-significant increase of PLTs count between the 3 studied groups (table 2), but there was a statistically significant rise of PLTs in heavy smokers compared to mild and moderate smokers (table 3). Similar findings have been documented by Mukta et al. [21] and Tulgar et al. [22], who reported an increase of PLTs count in smokers compared with non-smokers. while Jamsai et al. [20]found no change in PLTs count among smokers. This finding can be explained by the fact that smokers' thrombopoietin levels were higher than nonsmokers', promoting platelet production and resulting in higher platelet counts [23].

Smoking irritates the respiratory system, causing inflammation and release of inflammatory cytokines that can affect leucocyte proliferation, differentiation, and activation. Leucocyte counts are thought to be a separate risk factor for a variety of cardiovascular illnesses. There are conflicting findings from the multiple studies done to study how smoking affects differential leucocyte counts (DLC).In our study, there were statistically significant increases of monocyte% and statistically significant increases of TLC and neutrophil% ($p \prec 0.05$) among active smokers 'group when compared to passive smokers and nonsmokers' groups. While there has been statistically significant decrease of lymphocyte% in active smokers' group ($p \prec 0.05$), there have been no statistically significant differences between the studied groups with respect to absolute lymphocytes and eosinophil % (table2). Moreover, there were statistically significant rise of monocytes% ($p<0.001$), a statistically significant increase in TLC (p 0.017) and neutrophils (abs) ($p \prec 0.05$), a statistically significant decrease of lymphocytes% ($p \prec 0.05$), among active and passive smokers' groups. When comparing the active group to the control groups, there was a statistically significant increase of TLC (p 0.009), neutrophils, monocytes%, neutrophils (abs), with statistically significant reduction of lymphocytes% ($p \prec 0.05$). When comparing passive group to control group, there was a statistically significant increase of monocytes% (table 2). These findings pointed to the fact that either active or passive smokers develop inflammatory process. Additionally, In the current study, when we compared total and differential leucocyte count among mild, moderate, and heavy smokers, we found that there was a statistically significant increase of absolute neutrophil count ($p \prec 0.05$), whereas there was no significant difference in TLC, lymphocytes %, lymphocytes (abs), monocyte, eosinophil % and neutrophil % among heavy smokers subgroup compared to moderate and mild smokers subgroups (table 3),these results even it was disappointed but its open other route of researches over larger population to detect actual effect amount of smoking on TLC subpopulations. These results were matched with a study done by Claudine et al.[24]in which there has been a statistically significant rise of TLC count, particularly, lymphocytes and monocytes, among active smokers and secondhand smokers. The results corroborate with the results of Shipa et al.[25] and Sherke et al. [26]however, the study showed a significant difference in all types of TLC subpopulation among active smokers, secondhand smokers, and non-smokers. In the experimental research of Dinas et al.[27] it revealed significantly increased of TLC after an hour of exposure to secondhand smoke when compared to the initial value. The possible mechanism of leukocytosis in smokers is that nicotine triggers the release of catecholamine which can lead to elevation of TLC [25]. Tulgar et al.[22] also reported significant difference in monocyte and basophil count. Also, Shipa et al.[25],Vadapalli et al.[28] studies shown that an association between elevated TLC and cigarette smoking.

Nitric oxide and hydrogen peroxide, two free radicals produced by cigarette smoke, cause endothelial damage. Because of the oxidative stress that these free radicals produce, a systemic acute phase reaction is promoted. This reaction raises levels of inflammatory cytokines, CRP, fibrinogen, blood cell counts, total blood viscosity, and roulaux formation, which ultimately causes an elevation in ESR values [29]. In our research, smokers' ESR was non-significantly greater than that of non-smokers, ($p > 0.05$) (table 2). This result was matched with the results of Safia et al. [30], who found a non-significant difference in ESR levels in smokers in comparison with non-smokers. This contrasted with the findings of Sharma et al. [31] and Islam et al. [29], who found an increase of ESR in smokers than non-smokers. This increase was unrelated to the number of cigarettes smoked each day [31]) which also appear in our results (table 3) as there were no significant increase of ESR among the active smoker's group with

regard to smoking severity. Those results and our result may reflect the fact that ESR is affected by smoking practice either active or passive, but this conflict need further study on this point separately.

Also, CRP, another inflammatory marker, can be simply and accurately detected in a number of clinical circumstances to monitor the progression of disease, particularly in smokers [32]. Smokers have more TLC overall, primarily due to higher numbers of polymorphonuclear neutrophils that are recruited to inflammatory tissue after being released from the bone marrow. IL-β and IL-6, which are elevated in response to pulmonary inflammation and are thought to stimulate bone marrow cells, induce CRP gene expression[33].In our study we use CRP as inflammatory marker in smokers either active or passive and we found that there were significant increase of CRP (p 0.023) among active smokers compared to non-smokers (table 2).However, we did not find any difference of CRP between mild, moderate or heavy smokers (table 3). The same results were found by Maki et al. [19].Vadapalli et al. [34]and Khalid et al.[17] who concluded that smoking led to a large rise in serum CRP levels in smokers [35], came to the conclusion that although CRP levels are increased in current smokers, they are not correlated with the number of daily cigarettes smoked.

NLR is accepted as a systemic inflammatory marker, and in addition to being used to diagnose and determine the intensity of numerous diseases processes (including cardiovascular disease, lung diseases, infections, some malignancies, and endocrinological disorders), it has also been linked to prognosis, morbidity, and mortality[34]. The ratio is a new indicator reflecting platelet aggregation and burden of systemic inflammation. Both PLR and NLR have been the subject of many studies, and it has been suggested that they are relevant and may be prognostic markers for some cancer types such as lung and gastrointestinal[36]. The other important finding in the present study was that there were statistically significant increases of NLR (p 0.023), while there were no significant differences of PLR among the active group compared to other two groups (table 2).

There had been a statistically significant increase in NLR among the active smokers compared to passive and nonsmokers' groups (p 0.017 and0.001, respectively) (table 2). Tulgar et al.[22]reported increase of NLR in active smokers.

In our study as regards the correlation of smoking duration with Hb, HCT, RBCs count, RBCs indices and PLT in active and passive groups there was significant (p 0.003) positive connection (r 0.53) between duration of smoking and PLTs in active group. While there had been no significant connection between duration of smoking and Hb, HCT, RBCs count and RBCs indices in both active and passive group (table 4). These results in contrast with Mukta et al. [21] who found that there had been a positive connection between PLTs count and smoking duration. This correlation pointed that among PLTs is related to duration of smoking and among inflammatory markers obtained from CBC. NLR is the only markers affected by smoking duration, So PLTs and NLR can be used for follow up.

This study has some limitation that should be mentioned; first, subject even they were age and sex matched we didn't include the effect of age and sex (as hormonal parameter) in our results. Additionally, the number of studded groups were relatively low in relation to this public health problem.

CONCLUSION

Both active and passive smoking have adverse effect on hematological parameters, with more adverse effect in active heavy smokers when compared with mild, moderate smokers and passive smokers. CBC indices and inflammatory markers (CRP, ESR, PLR and NLR) are easily available, inexpensive and noninvasive methods for early detection of morbidity among smokers. Among inflammatory markers obtained from CBC; NLR is the most useful parameters for early detection of inflammatory process in smokers. Passive smokers are at risk for disturbance of blood indices, Hb level and inflammatory markers. We recommend follow up for healthy smokers either active or passive for early detection of hematological parameters abnormalities.

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الملخص العربي

مؤشرات تعداد الدم الكامل والبروتين التفاعلي سي في مدخني السجائر الأصحاء

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ملخص البحث:

الخلفية: يُعد تدخين السجائر مساهماً هاماً ومعروفًا في تطور العديد من الأمراض ذات مكون التهابي. للتدخين تأثيرات حادة ومزمنة على مؤشرات أمراض الدم.

الهدف:دراسة تأثير تدخين النشط والسلبى على مؤشرات تعداد الدم الكامل والبروتين التفاعلي سي.

الطرق:أجريت هذه الدراسة على 30شخصا سليما و مدخنًا نشطًا للسجائر و 30 شخصا سليما و مدخنًا سلبيًا و 30 شخصا سليما غير مدخنين كمجموعة ضابطة، جميع المجموعات كانوا متطابقين من حيث الجنس والعمر.تم تسجيل البيانات المتعلقة بالعمر والجنس ومؤشر ومدة التدخين وتم عمل فحص تعداد الدم الكامل، عدد كريات دم ابيض كلى و نوعي، نسبة الصفائح الدموية / الخلايا الليمفاوية، نسبة العدلات / الخلايا الليمفاوية، قياس سرعة الترسيب وبروتين التفاعلي سي.

النتائج: توجد فروق ذات دلالة إحصائية بين المدخنين النشطين والسلبيين وفقا لمعايير تعداد الدم الكامل عدا نسبة العدلات ومعدلات الالتهاب عدا سرعة الترسيب والبروتين التفاعلي سي، وبين المدخنين النشطين وغير المدخنين وفقا لمعايير تعداد الدم الكامل ومعدلات الالتهاب. بينما لا يوجد فرق إحصائي بين المدخنين السلبيين وغير المدخنين وفقا لمعايير تعداد الدم الكامل عدا نسبة الوحيدات ومعدلات الالتهاب عدا مسرعة الترسيب.

الاستنتاجات: كلا من التدخين النشط والسلبي لهما تأثير سلبي على معايير الدم ومعدلات الالتهاب.

الكلمات المفتاحية: التدخين، تعداد الدم الكامل، التدخين النشط، التدخين السلبي، آثار التدخين.

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