Combined effect of workplace noise and smoking on some hematological parameters on workers in a food manufacturing plant

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ABSTRACT

Generally, no industry can be found to be safe in terms of noise pollution. Noise is the wide- spread form of environmental stressor in the industrialized urban areas.

Aim: the purpose of this paper is to evaluate the combined effect of workplace noise and smoking on some hematological parameters on employing work in a food manufacturing plant.

This is a retrospective study before and after for five years since starting of the work. In this study, 50 male subjects participated: smokers (n=11) and nonsmokers (n=39), for further individual information and certain specific points, a developed standard questionnaire, were filled out by participants. For the past 4-year's details, blood tests and medical records of persons since initially hired, were used. The details of the fifth year were measured by the presenters. Using the ISO protocol 1999 and 9612, workplace noise was measured and the noise map was drawn using arc-view GIS software. Statistical analysis SPSS software version 18 was investigated. Due to the nature of the study, the significance level was set at a P value ≤ 0.1.

Statistical findings and laboratory data showed that the effect of noise and smoking on red blood cells and white blood cells of smokers and nonsmokers was significant ($p<0.1$), so that the amount of red blood cells in smokers who are exposed to noise exceeding 88.83 dB, is higher than nonsmokers, and the white blood cells are lower in nonsmokers in compared with smokers.

Our findings showed that combined of workplace noise and smoking has severe adverse effects on hematological parameters, and these alterations might be associated with a greater risk for more diseases. It is notable that results are from a research effort of its researchers and it is not completely certain so further investigation will be needed.

Key words: Hematocrit, Hematological, Hemoglobin, Smoking, Work Place Noise

INTRODUCTION

Generally, no industry can be considered to be safe in terms of noise pollution [1]. Noise is the most widespread form of environmental stress or in the industrialized urban areas [2].

The term "stress" for the first time, was used in physiology by cannon in 1939. Response to stress, including changes in blood glucose and electrolytes, changes in the number of white blood cells, hyper adrenal hypertrophy, changes in the thymus and etc. [3]. Various studies have shown that stress has some effects on human such as effect on the cardiovascular system and blood parameters [4]. For years, the harmful effects of loud noise are known as a cause of stress and physiological and psychological changes in humans [5]. Noise exposure exceeded from 85 dB in any form beyond, known as a source of stress [6] and since noise is known as one of the most important adverse physical factors at work [7]., It has adverse effects on living organisms and biological systems in addition to hearing loss, that have been reported systematically, and has some adverse effects on heart, liver, blood and reproductive system [6, 8-13]. Finally, non – auditory effects of noise, including the effects of physiological and psychological those have interfered with body functions and its activities [14].

The effects of cigarette smoking on human health are serious and in many cases deadly. [15] Tobacco cigarette smoking is part of the major leading causes of death and essential public health challenge in the world over [16-17]. There are greater than 4000 chemicals found in cigarette smoke [18], and a cigarette smoker is exposed to a number of harmful substances including nicotine, free radicals, carbon monoxide and other gaseous products [19]. It is well known that smokers have a higher risk for cardiovascular diseases, hypertension, inflammation, stroke, clotting disorder, and respiratory disease [20-26].

Moreover, cigarette smoking accelerates pathogenesis in different type of cancers such as lung, pancreas, breast, liver and kidney [17, 21- 22].Tobacco smoking has been correlated to cause several major morphological and biochemical problems in individuals. Smoking has both acute and chronic effects on hematological parameters [15] during the past decade. It was suggested that cigarette smoking affects the blood characteristics as well that leads to death. For example, the relation between smoking and white blood cell count has been clearly established [20, 22-23]. In a number of studies, it has been found that smokers have a higher white blood cell counts than nonsmokers (21, 24, 26), although in some earlier studies relationship between smoking and red blood cell was found in smokers [27].

Although the effects of smoking on blood parameters are known, and also the effect of noise on the auditory system is proven, however, few studies taken on the effect of noise on other organs such as the cardiovascular system and blood , as the effect of noise on different parameters of cardiovascular and blood is conflicting and uncertain [28]. So in view of this report, we reviewed and analyzed the combined effect of workplace noise and smoking on some hematological parameters of employed who have worked in a food manufacturing plant (Iran–Abhar).

MATERIALS AND METHODS

This is a retrospective (before and after) study for five years since beginning of the work. In fact, prior to employment, the situation was control and 5-year period is a case situation. This sectional–retrospective study been composed of two stages required to demographic data and information about confounding factors, and retrospective studies under field conditions.

In order to measure workplace noise, first reviewed existing work focuses on noise sources, acoustical measurement using the methods and protocols of ISO 1999 and ISO 9612, in a flour workshop with size of 300 square meters; consist of Rotary Sieve flour machines and Winding machine for flour, has done. By selecting methods, 23 measuring stations determined, and during the 8-hour shifts, using Mastech Sound Level meter model 760 type 1, Leq (dB) was calculated, and then workplace noise map using arc view GIS software plotted. Using the noise map, scattering people in the workplace was reviewed during a shift work and the noise received by each sample, was measured by the dosimeter TES1354. Values obtained from individual dosimeter and workplace noise measurement, were equal amounts, therefore the values obtained for data analysis were used for work place noise measurement. It should be noted that the time of measuring was day, and during the shift work in a situation where all the devices were turned on and the workers were working.

Finally, all subjects, population of 50 people were enrolled. In order to be aware of some specific items and personal information that were likely to interfere with the consequences, a questionnaire has been completed by the subjects. This valid questionnaire has been agreed in consultation with specialists in hematology and occupational medicine. Requirements such as: age, gender, weight, work experience, marital status, shift work system, following the special diet, smoking, certain diseases, anemia, regular use of medication, drugs and etc., were requested in the questionnaire. therefore , exclusion criteria of the study included : lack of physical and mental health, alcohol consumption, use of sleep medications and certain drugs such as : streptomycin, gentamycin, quinine, salicylates, paromomycin, neomycin, rifampin (toxic labyrantitis), continuous use of antibiotics, blood diseases, surgery in the past 6 month prior of blood test, blood receive or donation shortly before blood test and shift work, so after completing the questionnaire , these cases were investigated.

By aware of confounding factors on blood parameters, including fasting during blood test, vigorous activity for 15 minutes before test, blood receive or donation shortly before the blood test, surgery 6 months prior of blood test, cold at time of testing, and after determining the sample size and selection of all the participants who exposed to the workplace noise, exceeded from 85 dB, blood samples were taken. Because it was a retrospective study, to access the data in the last 4 years, the information contained in their medical records, which regularly completing and monitoring every year, has been used.

Blood samples received by the fifth year, were analyzed using system kx21 cell counter in the medical laboratory of the plant and then hematological parameters including red blood cells based on (mli/µL), white blood cells according to (count/µL), hemoglobin in terms of (g/dL) and percentage of hematocrit were evaluated.

All periodic testing in this series is from the beginning of employment (initial experiments) and samples which has been updated in recent years. This is a before and

after study, it means that the combined effect of workplace noise and smoking on blood parameters has been measured in one group of people for 5 years. The advantages of this approach are reduction of sample size, reduction of individual differences and reduction of potential errors and confounding factors.

After the data collection phase, and ensure the normal distribution of variables through the one- sample Kolmogorov Smirnov test and statistical analysis such as chi–square , Cochran and Mantel–Haenzel, and by spss software version 18, the combined effects of workplace noise and smoking on some hematological parameters were evaluated. Because of the retrospective nature of the study, a significant level was considered $p_{value} \leq 0.1$.

RESULT

In this study, 50 employees participated from the flour workshop of a food manufacturing plant. Given the demographic characteristics, the male gender dominance in the workshop, so in consultation with a statistician, a measure of gender factor with other parameters was negligible. Based on the results obtained from the data provided in the questionnaire, from 50 subjects participated in the study, 11 (22%) were smokers and 39 (78%) were nonsmokers. Workplace noise measurement showed that workers worked in 8-hour shift work have been exposed to an average of 88.83±1.30219 dB Leq(Table 1) .To determine the distribution of workstations and workplace noise exposure, noise map was plotted (figure 1).

Table 1: Description of the quantitative variables and average values of parameters during 5 years.

Type of variable	Average (Standard deviation)	The minimum amount	The maximum amount	Total number	Unit
Workplace noise	88.83 (1.30)	86.50	90.50	50	dB
Average of red blood cells during 5 years	5.44 (0.34)	4.62	6.37	50	mli/µL
Average of white blood cells during 5 years	6730.00 (1145.82)	4880.00	10960.00	50	count/µL
Average of hemoglobin during 5 years	15.46 (0.89)	12.50	17.40	50	g/dL
Average of hematocrit during 5 years	45.90 (2.18)	40.26	51.28	50	%

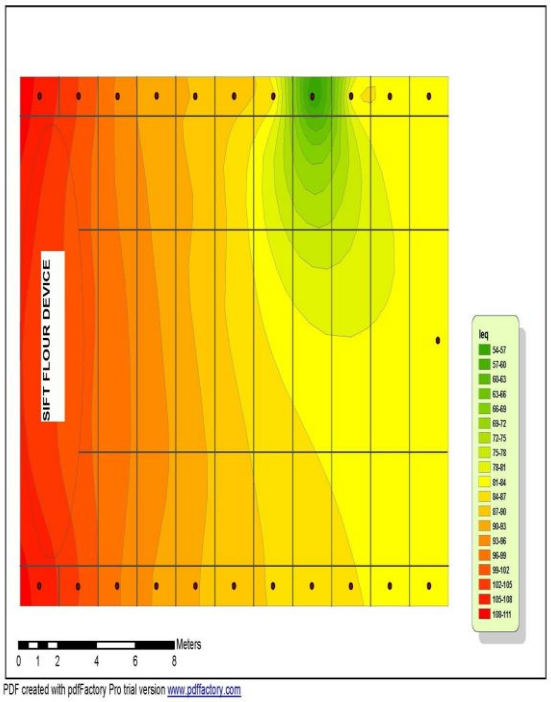

Fig.1: Noise map drawing arc view GIS

Figures 2 to 5 represent moderate changes in hematological parameters; red blood cells, white blood cells, hematocrit and hemoglobin during 5 years of noise exposure in equivalent sound level of 88.83 dB. The results of blood tests during the 5- year average are given in table 1. As showed in figures 2 to 5, the trend of the average amount of blood parameters in the last 5 year has been upward.

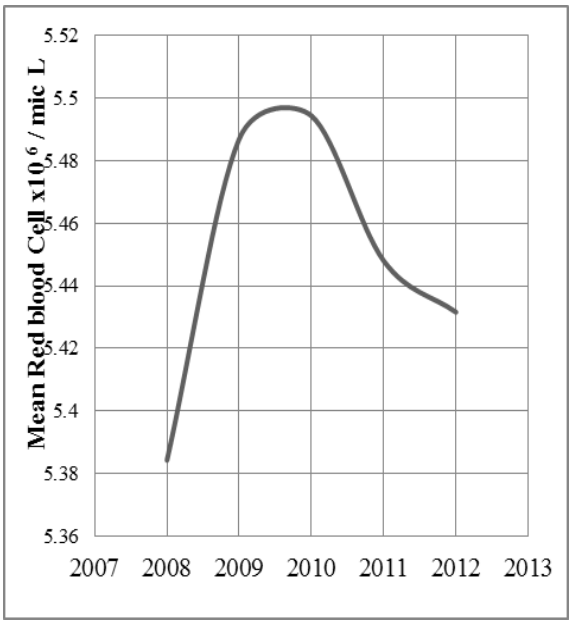

Fig.2: Trend of red blood cells average during 5 years

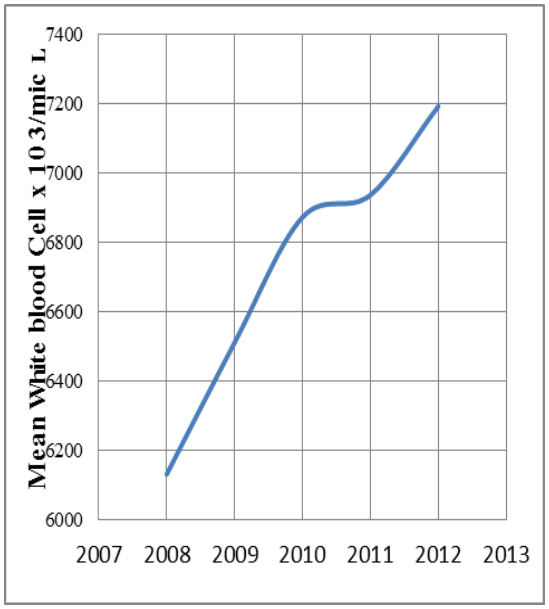

Fig.3: Trend of white blood cells average during 5 years

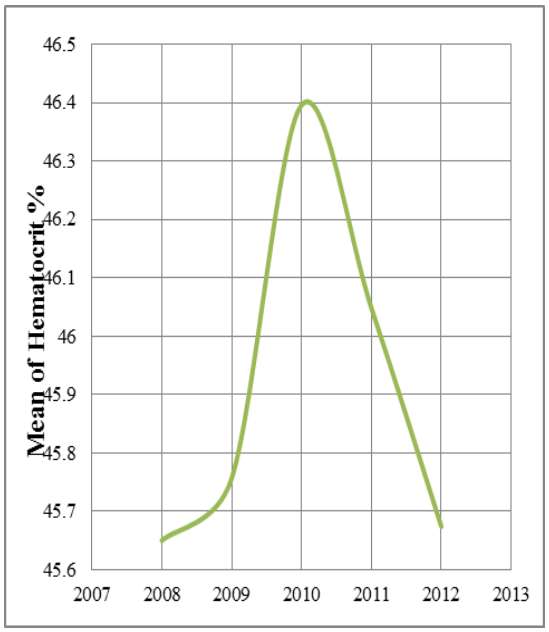

Fig. 4: Trend of hematocrit average during 5 years

Based on the results in table 2 , the average value of each blood parameters such as ; the average amount of red blood cells , white blood cells , hematocrit and hemoglobin in smokers are higher than nonsmokers during 5 years but the differences were not significant ($p \geq 0.1$).

Table 3 to 6 represents the relation between the combined effect of workplace noise and smoking on some hematological parameters using chi–square, Cochran and Mantel–Haenzel tests.

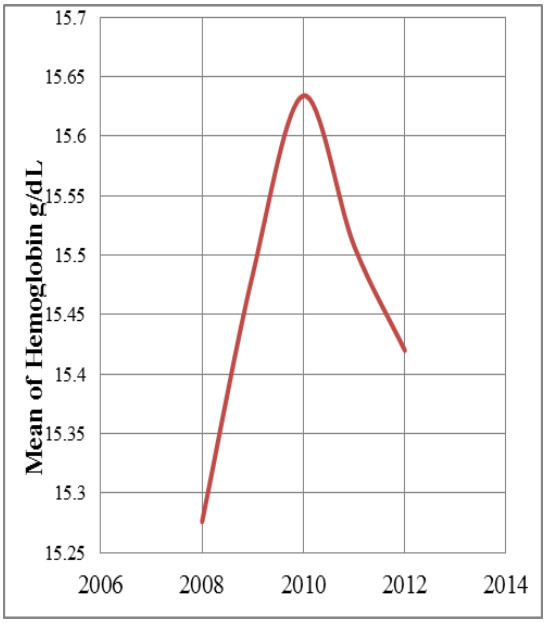

Fig.5: Trend of hemoglobin average during 5 years

Table 2: The relationship between blood parameters in smokers and nonsmokers using the t-test

indices / Blood parameters/ smoking		average	Standard deviation	Statistical tests (t-test)	
Average of red blood cells during 5 years (mli/µL)	smoker	5.56	۰،۳۸	P_{value}e=0.32	T= 1.00
	nonsmoker	5.42	۰،۳۳		
Average of white blood cells during 5 years (count/ µL)	smoker	7012.72	1511.82	P_{value}=0.35	T=0.92
	nonsmoker	6650.25	1030.45		
Average of hematocrit during 5 (%) years	smoker	46.56	1.63	P_{value}=0.25	T=1.14
	nonsmoker	45.71	0.36		
Average of hemoglobin during 5 (g/dL) years	smoker	15.74	0.64	P_{value}=0.24	T=1.17
	nonsmoker	15.38	0.95		

As shown in table 3, the effect of noise and smoking on red blood cells of smokers and nonsmokers was significant ($p \leq 0.05$), so that the amount of red blood cells in smokers, who are exposed to noise exceeding 88.83 dB, is higher than nonsmokers.

Table 4 shows the relationship between the combined effect of noise and smoking on the average of white blood cells during 5 years. Based on results, the average amount of white blood cells in nonsmokers and smokers shows

a significant difference ($p_{value} \leq 0.1$) it means that the average value of the white blood cells of nonsmokers is lower than smokers. According to the findings in table 5 and 6, the relationship between the workplace noise and smoking effects on hematocrit and hemoglobin for 5 years has been analyzed and no significant difference was observed ($p \geq 0.1$).

Table 3: Relation between combined effect of workplace noise and smoking on red blood cells (mli/μL) using chi–square, Cochran and Mantel–Haenzel tests.

tests		χ_{chi}	P_{value}
Chi-square	smoker	3.59	0.05
	Nonsmoker	0.19	0.65
Cochran		1.53	0.21
Mantel-Haenzel		0.86	0.35

Table 4: Relation between combined effect of workplace noise and smoking on white blood cells (μL/count) using chi–square, Cochran and Mantel–Haenzel tests.

tests		χ_{chi}	P_{value}
Chi - square	smoker	0.05	0.81
	nonsmoker	3.72	0.05
Cochran		3.29	0.06
Mantel-Haenzel		2.22	0.136

Table 5: Relation between combined effect of workplace noise and smoking on hematocrit (%) using chi–square, Cochran and Mantel–Haenzel tests.

tests		χ_{chi}	P_{value}
Chi - square	smoker	0.35	0.55
	nonsmoker	0.55	0.45
Cochran		0.87	0.35
Mantel-Haenzel		0.39	0.52

Table 6: Relation between combined effect of workplace noise and smoking on hemoglobin (g/dL) using chi–square, Cochran and Mantel–Haenzel tests.

tests		χ_{chi}	P_{value}
Chi - square	smoker	2.21	0.13
	nonsmoker	1.29	0.25

DISCUSSION

This study investigated the combined effects of workplace noise and smoking on hematological parameters on whom working in a food manufacturing plant. Experimental and statistical results such as t- test, Chi–square, Cochran and Mantel–Haenzel showed significant differences in hematological parameters.

Based on the findings, the workplace noise and cigarette smoking both increase the amount of red blood cells over 5 years, and are consistent with other investigations [16, 27, and 29]. A general increase for red blood cells occurs in such a situation; the body compensates for the lack of oxygen in the poor performance of heart and lungs, lack of oxygen high altitude areas, reduction of blood plasma, smoking and stress [30]. It is pointed out that high level RBC (red blood cell) associated with blood viscosity and clotting in smokers [31-33]. High level of RBC is termed as polycythemia and very high RBC mass shows blood viscosity and increase the risk of intravascular clotting. Coronary vascular resistance decreased coronary blood flow, and a predisposition to thrombosis [34].

As noise as a stressor and smoking , both are causing increased blood viscosity, increase blood pressure , increase risk of cardiovascular diseases and increase amount of red blood cells , It has been estimated that the increasing risk of cardiac disease in smokers who have exposed to high level of workplace noise , may be associated with high fibrinogen levels through arterial wall , inflammation and effects on blood velocity, palette aggregation and fibrin formation [24, 35-36].

Although strong epidemiological evidence links cigarette smoking to cardiovascular disease, cancer and chronic obstructive pulmonary disease (COPD), the exact mechanisms of these links remain poorly understood [15] some of the adverse effects of smoking include initiation of endothelial injury [37], acceleration of coronary progression and new lesion formation [38] and overall alternations in lipid and hemostatic systems [39]. Detecting endothelial damage may be the most useful step in the early diagnosis of atherosclerosis although the endothelium releases many molecules into the circulation and the arterial wall , not all of them are specific to the endothelium and therefore of limited research or diagnostic potential [40].

White blood cell count is perhaps the most useful, inexpensive and simple biomarker for endothelial damage [15] we found that nonsmokers who exposed to high level work place noise had significantly lower white blood cell count compared to smokers in a same condition ($p \leq 0.1$). On the other hand, it means that the white blood cell count in smokers is higher than nonsmokers. The high

white blood cell count of smokers in this study is consistent with other published reports [25, 41]. Freedman *et al.* observed the median total white blood cell count was 36% higher in current smokers as opposed to nonsmokers [24]. The mechanism for smoking- induced increase in white blood cell count is not clear [15] it has been suggested that inflammatory stimulation of the bronchial tract induces an increase in inflammatory markers in the blood [42-43]. While blood cell may simply be a marker of smoking- induced tissue damage, the high count can promote cardiovascular diseases through multiple pathological mechanisms that mediate inflammation, plug the microvasculature, induce hyper coagulability and promote infarct expansion [17,20,25-27,29,37-43]. In fact, several studies have shown that white blood cell count is an independent predictor of atherosclerosis and cardiovascular disease [44-45].

According to table 5 and 6, combined effects of workplace noise and smoking on the mean value of hematocrit and hemoglobin during 5 years showed no significant difference ($p \geq 0.1$), the obtained results with previous studies [15-15, 26-27] that believe the effects of smoking increased hematocrit and hemoglobin because of the increase in carbon monoxide in the blood, are not in agreement.

Finally, the high white blood cell count and red blood cell in our smoking subjects who were exposed to workplace noise, may also suggest that they might be at greater risk for developing high blood viscosity atherosclerosis and cardiovascular diseases. Thus, it can be concluded that workplace noise and smoking, both, have synergistic effects on red blood cells and white blood cells.

CONCLUSION

This scientific study is the result nature of multiple causes of non – auditory effects of noise and because of the results observed in this study, these effects cannot be definitively attributed to the noise or it cannot be completely innocent, so several studies with different designs should be done to obtain results that are more precise. It is noted that the results are from the research effort of its researchers and it is not completely certain so further investigation is needed of logical, profound and practical – theoretical focus research, which has been prepared and published by enforcement efforts with a new approach to achieve new results, however, due to the.

REFERENCES

[1] Attari S, Golmohammadi R, Saremi M. The study of the relationship between the level of noise exposure and NIHL other related complications Workers Malayer stamping factory, the Iranian Congress of Occupational Health, Hamadan, 1383; 377-37[Persian].

[2] Archana R, Namasivayam A. The effect of acute noise stress on neutrophil functions, Indian J Physiol Pharmacol 1999; 43 (4): 491-95.

[3] Sele H. The general adaptation syndrome and diseases of adaptation. J Clin Endocrinol 6 .1959; 117-30.

[4] Ahmadi H, Rostami P. The effect of restraint stress in pregnant rats on blood parameters of their off springs, physiology and pharmacology.2008; 12 (1), 76-82 . [Persian]

[5] Rom WN. Environmental and occupational medicine. 3rd ed. Phlidephia: lippincotte-raven press ; 1998;1345-49.

[6] Ravindran RD, Samson J, Sentlivelan M. Noise- stress induced brain neurotransmitter changes and the effect of ocimum sanctum (Linn) treatment in albino rats. J pharmacol sci 2005; 98(4):354-6.

[7] Mate JM, perez – Gomez C, Nunez de Castro I. Antioxidant enzymes and human diseases. Clin Biochem 19999; 32(8): 595-603.

[8] Pinar T, Atli AK, Alacam H, *et al*. The effects of noise on oxidative and antioxidative balance in human erythrocytes. inter j hematol oncol 2011;21(1),27-37.

[9] Mates JM, perez-gomez C, nunez DE castro I. Antioxidant enzymes and human diseases clin biochem 1999;32(8):595-03.

[10] Abate C, Concetlo G, Fortumato M, et al. Influence of environment factors on the evolution of industrial noise- induced hearing loss: environ monit assess 2005;107 (1-3), 351-61.

[11] Lenzi P, Frenzilli G, Gesi M, *et al.* DNA damage associated with ultra structural alternations in rat myocardium after loud noise exposure, environ health perspect 2003; 111(4): 467-71.

[12] Stansfeld SA, Matheson MP. Noise pollution non auditory effects on health. Br med bull 2003; 68: 243-57.

[13] Demirel R, Mollaoglu H, Yesiyurt H, *et al.* Noise induces oxidative stress in rat. Eur j general med 2009;6(1):20-24.

[14] Motamed zade M, Ghazaeie S. Combined effects of noise and shift work on physiological parameters on workers in chemical industry. Hamedan university of medical sciences journal, spring 2003; 39. [Persian].

[15] Asif M , Sajjad K, Zubaida U, Arif M. Effect of cigarette smoking based on hematological parameters: comparison between male smokers and nonsmokers. Turkish Journal of Biochemistry–Turk J Biochem] 2013; 38 (1); 75–80.

[16] Kume A, Kume T, Masuda K, Shibuya F, Yamzaki H. Dose-dependent effect of cigarette smoke on blood biomarkers in healthy volunteers: Observations from smoking and non-smoking. Journal of Health Sciences 2009; 55(2):259-64.
[17] Islam MM Amin MR, Begum S, Akther D, Rahman A. Total count of white blood cells in adult male smokers. J Bangladesh Soc Physiol 2007; 2:49-53.
[18] Green CR, Rodgman A. The tobacco chemists' research conference: a half century forum for advances in analytical methodology of tobacco and its products. Recent Adv Tobacco Sci 1996; 22:131–04.
[19] Gitte RN. Effect of cigarette smoking on plasma fibrinogen and platelet count. Asian Journal of Medical Sciences 2011; 2:181-84.
[20] Abel GA, Hays JT, Decker PA, Croghan GA, Kuter DJ, et al. Effects of biochemically confirmed smoking cessation on white blood cell count. Mayo Clin Proc 2005; 80(8):1022-28.
[21] Yarnell JW, Baker IA, Sweetnam PM, Bainton D, Obrien JR,et al. Fibrinogen, viscosity and white blood cell count are major risk factors for ischemic heart disease. The Caerphilly and Speedwell collaborative heart disease studies. Circulation 1991;83:836-44.
[22] Carel RS, Eviatar J. Factors affecting leukocyte count in healthy adults. Preventive Medicine 1985; 14:607-19.
[23] Torres de Heens GL, Kikkert R, Aarden LA, Velden Van der U, Loos BG. Effects of smoking on the ex vivo cytokine production.J Periodont Res 2009; 44:28-34.
[24] Wannamethee SG, Lowe GD, Shaper AG, Rumley A, Lennon L, et al. Association between cigarette smoking, pipe/cigar smoking, and smoking cessation, haemostatic and inflammatory Markers for cardiovascular disease. Eur Heart J 2005; 26(17):1765-73.
[25] Freedman DS, Flanders WD, Barboriak JJ, Malarcher AM, Gates L. Cigarette smoking and leukocyte sub population in men.Ann Epidemol 1996; 6(4):299-06.
[26] Tiel D, Van EL, Peeters HMP, Smit AH, Nagelderke JDN, Loon MVAJ, et al. Quitting smoking may restore hematological characteristics within five years. Ann Epidemiol 2002. 12:378-88.
[27] Tarazi IS, Sirdah MM, El Jeadi H, AlHaddad RM. Does cigarette smoking affect the diagnostic reliability of hemoglobin a2d2 (HbA2). J Clin Lab Ana 2008; 22:119–22.
[28] Ghazaeie s. combined effects of noise and shift work on blood pressure in tire industry, Hamedan university of medical sciences journal, spring 2003; 27: 39. [Persian].
[29] Bain BJ, Rothwell M, Feher MD, Robinson R, Brown J, et al. Acute changes in haematological parameters on cessation of smoking. J Royal Soci Med 1992; 85:80-82.
[30] http://www.shahrekhabar.com/medical/138073140048031
[31] Ho CH. White blood cell and platelet counts could affect whole blood viscosity. J Chin Med Assoc 2004; 67(8):394-97.
[32] Simpson AJ, Gray RS, Moore NR, Booth NA. The effects of smoking on the fibrinolytic potential of plasma and platelets. Br J Haematol 1997; 97:208-13.
[33] Levenson AC, Simon FA, Cambien and C Beretti. Cigarette smoking and hypertension. Factors independently associatedwith blood hyperviscosity and arterial rigidity. Arterioscler Thromb Vasc Biol. 1987; 7:572-77.
[34] Ravala M and Paula A. Cerebral venous thrombosis and venous infarction: Case report of a rare initial presentation of smoker's polycythemia case rep. Neurol 2010; 2:150–56.
[35] Hunter KA, Garlick PJ, Broom I, Anderson SE, McNurlan MA. Effects of smoking and abstention from smoking on fibrinogensynthesis in humans. Clin Sci 2001; 100:459 -65.
[36] Danesh J, Collins R, Peto R, Lowe GD. Haematocrit, viscosity,erythrocyte sedimentation rate; meta-analysis of prospective studies of coronary heart disease. Eur Heart J 2000; 21:512-20.
[37] Pittilo RM. Cigarette smoking, endothelial injury and cardiovascular disease. Int J Exp Pathol 2000; 81:219–30.
[38] Waters D, Lesperance J, Gladstone P, Boccuzzi ST, Cook T, Hudgin R, Krip G, Higginson L. Effects of cigarette smoking on the angiographic evaluation of coronary atherosclerosis: a Canadian Coronary Atherosclerosis Intervention Trial (CCAIT) substudy. Circulation 1996; 94:614–21.
[39] Tsiara S, Elisaf M, Mikhailidis DP. Influence of smoking on predictors of vascular disease. Angiology 2003; 54:507–30.
[40] Blann AD, Lip GY. The endothelium in atherothrombotic disease: assessment of function, mechanisms and clinical implications.Blood Coagul Fibrinolysis. 1998; 9:297–06.
[41] Kawada T. Smoking-induced leukocytosis can persist after cessation of smoking. Arch Med Res 2004; 35:246–50.
[42] Calapai G, Caputi AP, Mannucci C, Russo AG, Gregg E, Puntoni R, Lowe F, McEwan M, Bassi A, Morandi S, and Nunziata A. Cardiovascular biomarkers in groups of established smokers after a decade of smoking. Basic & Clinical Pharmacology & Toxicology 2009; 104:322–28.
[43] Geffken D, Cushman M, Burke GL, Polak JF, Sakkinen PA, Tracy RP. Association between physical activity and markers of inflammation in a healthy elderly population. Am J Epidemiol 2001; 153:242–50.

[44] Madjid M, Awan I, Willerson JT, Casscells SW. Leukocyte count and coronary heart disease: implications for risk assessment.J Am Coll Cardiol 2004; 44:1945–56.
[45] Loimaala A, Rontu R, Vuori I, Mercuri M, Lehtimaki T, Nenonem A, Bond MG. Blood leukocyte count is a risk factor for intimamedia thickening and subclinical carotid atherosclerosis in middle-aged men. Atherosclerosis 2006; 188:363–69.