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The Effect of Cigarette Smoking on Blood Parameters and Serum Minerals on Smoker's Women in Basrah (Iraq)

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Abstract

Introduction. Cigarette smoking is a common cause of health problems. To date, the adherence to smoking in women, as well as the specific effects of smoking on the morphological composition of the blood and the content of certain minerals in it, depending on the age of smokers, remain insufficiently studied.
Purpose. To compare the effect of cigarette smoke on some hematological parameters and minerals between smoker and non-smoker women.
Materials and methods. Samples of whole blood and serum of volunteers were studied, among whom were 20 smokers and 14 non-smokers aged from 20 to 40 years; smokers were divided according to smoking experience into two groups – 1–15 years and 16–30 years. The work used an automated method for studying the content of blood cells (erythrocytes, platelets, leukocytes with the establishment of the average volume of erythrocytes and taking into account the hemoglobin content) on a hematological autoanalyzer, as well as photometric methods for determining the content of serum iron, magnesium, total calcium, zinc.
Results. The result of this study showed significant differences in red blood cell count, hemoglobin, platelet count and mean cell volume between female smokers and non-smokers, while there was no statistically significant difference in white blood cell count was not found. Against this background, a significant decrease in the concentration of calcium, magnesium, and zinc was revealed in smoking women compared to non-smokers, while the concentration of iron increased significantly. In a smoking history of 16–30 years, changes in the content of blood cells and the elemental composition of blood serum were significantly more pronounced both in relation to those in the control group of persons and in relation to the contingent of women with less smoking experience: 1–15 years.
Conclusion. Cigarette smoking affects hematological parameters and blood elemental composition (including trace elements) in women who smoke compared to non-smokers. Changes in the parameters of morphological blood elements and the content of the studied mineral substances turned out to be significantly more pronounced in women with a long history of smoking.
Keywords: cigarette smoke, blood counts, nutrients, non-smokers, trace elements, hematological parameters

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Влияние курения сигарет на гематологические параметры и минеральный состав сыворотки у курящих женщин в Басре (Ирак)

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Резюме

Введение. Курение сигарет является распространенной причиной возникновения проблем со здоровьем. К настоящему времени остаются недостаточно изученными приверженность к курению женщин, а также особенности его влияния на морфологический состав крови и содержание в ней отдельных минеральных веществ в зависимости от возраста.
Цель. Сравнить влияние курения сигарет на некоторые гематологические параметры и минералы у курящих и некурящих женщин.
Материалы и методы. Исследованы образцы цельной крови и сыворотки добровольцев, среди которых были 20 курящих и 14 некурящих в возрасте от 20 до 40 лет, курильщицы были разделены по стажу курения на две группы – 1–15 лет и 16–30 лет. В работе использованы автоматизированный метод исследования содержания форменных элементов крови (эритроцитов, тромбоцитов, лейкоцитов с установлением среднего объема эритроцитов и учетом содержания гемоглобина) на гематологическом автоанализаторе, а также фотометрические методы определения содержания сывороточного железа, магния, общего кальция, цинка.
Результаты. Результат этого исследования показал значительные различия в содержании эритроцитов (RBC), гемоглобина (Hb), тромбоцитов (PCV) и показателях среднего объема эритроцитов (MCV) у курящих и некурящих женщин, в то время как статистически значимой разницы в содержании лейкоцитов (WBC) обнаружено не было. На этом фоне выявлено значительное снижение концентрации кальция, магния, цинка у курящих женщин по сравнению с некурящими, в то время как концентрация железа значительно повысилась. При стаже курения 16–30 лет изменения в показателях содержания форменных элементов крови и элементном составе сыворотки крови были значительно более выраженными как по отношению к таковым в контрольной группе лиц, так и по отношению к контингенту женщин с меньшим стажем курения – 1–15 лет.
Заключение. Курение сигарет влияет на гематологические параметры и элементный состав крови (включая микроэлементы) у курящих женщин по сравнению с некурящими. Изменения в показателях морфологических элементов крови и содержании исследованных минеральных веществ оказались значительно более выраженными у женщин с большим стажем курения.
Ключевые слова: сигаретный дым, показатели крови, нутриенты, некурящие, микроэлементы, гематологические показатели

■ INTRODUCTION

Smoking a cigarette is a bad habit that and one of essential causes leading to a complicated disease and die all over the world [1]. Approximately, four millions smoker died every year and this number will increase to more than 8 million by 2030 according to WHO reports [2]. Smoking is defined as inhalation of burning tobacco which is either occasional habit or a consequence of nicotine inhalation addiction [3]. Cigarette smoking causes the killing of more than half million smoker women around the world and this number is in rapid increase in the period between 1950–2000 to about ten million in many countries [4, 5].

There are more than 4000 different chemicals in every single cigarette smoke, 200–400 are known as toxic or carcinogens. These are nicotine, tar, carbon monoxide, nitrogen oxides, free radicals and some oxidants [6, 7].

Many studies suggested that smoking cigarette can affect the blood parameters [6, 8], found significant increase in WBC counts [9, 10], increase in hemoglobin concentration [11, 12]. Several investigators have described the effect of smoking cigarette on minerals and electrolytes, zinc concentration significantly reduce in smoker [13]. Other researchers demonstrated that smoking cause increase in level of serum iron and decrease of magnesium and calcium among smoker [14–16].

■ PURPOSE OF THE STUDY

To compare the effect of cigarette smoke on some hematological parameters and minerals between smoker and non-smoker women.

■ MATERIALS AND METHODS

Sample collection

This study was carried out on 34 volunteer women aged 20–40 years. Fourteen nonsmoker women and 20 smokers. All volunteer underwent medical health diagnosis at Al-Sadder Educational Hospital. A questionnaire was planned to obtain information as age, habitat (smoker or non), the number of cigarette smoker per day, smoking time (1–15 and 16–30) years and the health condition. All blood samples were collected at the morning after an overnight fasting, 7 ml of venous blood withdrawn. CBC counts were estimated and the serum was separated and used for estimation of serum (zinc, magnesium, iron and calcium).

Iron concentration

It was determined by using kit from biolabo France according to the colorimetric method approved [17]. The concentration of iron calculated as follow: (Iron μg/dl) = absorbance of serum (A2-A1) / absorbance of standard (A2-21) xst.con.

Magnesium concentration

It was determined by using kit from spectrum Egyptian according to the colorimetric method approved [18]. The concentration of magnesium calculated as follow: (magnesium mg/dl) = absorbance of serum / absorbance of standard × standard concentration.

Calcium concentration

It was determined by using kit from Randox United Kingdom according to the colorimetric method approved [19]. The concentration of calcium calculated as follow: (calcium mg/dl) = absorbance of serum / absorbance of standard × standar concentration.

Zinc concentration

It was determined by using kit from ILTA-ITALY. The concentration zinc of calculated as follow: (zinc μg/dl) = absorbance of serum / absorbance of standard × 200.

Statistical analysis

Statistical Package of Social Sciences Version 23 (SPSS.V.23). Data normality were tested used Shapiro test. Independent t-test was performed to analyze the data. The significant differences were determined using $p \leq 0.05$.

■ RESULTS

Table 1 showed the variation in blood parameters between smoker and non-smoker women. A significant increase in some blood parameters in smoker women. RBC increased significantly ($p \leq 0.05$) in smoker women ($6.1 \pm 6.1 \times 10^6$/μL) in comparison in non-smoker ($5 \pm 1.23 \times 10^6$/μL). A significant increase in Hb in smoker women (14.20±0.24 g/dl) while it was (10.79±0.21 g/dl) in non-smoker. PCV apparent significant raised in smoker women (39.65±0.33%) in comparison with non-smoker (31.43±0.4%). MCV was (81.86±1.27 μm^3) in non-smoker while in smoker recorded (101.1±0.86 μm^3). WBC was not significantly changes. According to the period of smoking the table 2 showed significant increased ($p \leq 0.05$), in the period (16–30) in comparison with the period (1–15) year of smoking.

Table 3 showed significant increased ($p \leq 0.05$), in serum iron in smoker women (82.15±2.92 μg/dL). Calcium in smoker women showed a significant decrease (6.91±

Table 1
Difference in blood parameters between cigarette smoker women and non-smoker (mean±SE)

Groups	WBC ($\times 10^3$/μL)	RBC ($\times 10^6$/μL)	Hb (g/dl)	PCV (%)	MCV (μm^3)
Non-smoker	6.25±4.6[a]	5±1.23[a]	10.79±0.2[a]	31.43±0.4[a]	81.86±1.27[a]
Smoker	6.79±1.42[a]	6.1±6.1[b]	14.2±0.24[b]	39.65±0.33[b]	101.1±0.86[b]

Notes: [a, b] different letters refers to significant difference $p \leq 0.05$.

Table 2
Difference in blood parameters according to the period of smoking (mean±SE)

Groups	WBC ($\times 10^3$/μL)	RBC ($\times 10^6$/μL)	Hb (g/dl)	PCV (%)	MCV (μm^3)
1–15 year	6302.5±91.77[a]	5900.6±43.22[a]	13.4±.22[a]	38.5±0.24[a]	98.5±0.4[a]
16–30 year	7278.2±156.52[b]	6313.5±69.7[b]	15±.25[b]	40.8±.24[b]	103.7±1.21[b]

Notes: [a, b] different letters refers to significant difference $p \leq 0.05$.

Table 3
Minerals (iron, magnesium, calcium and zinc) in serum of cigarette smoker women and non-smoker (mean±SE)

Groups/ parameters	Iron (μg/dL)	Calcium (mg/dL)	Magnesium (mg/dL)	Zinc (μg/dL)
Non-smoker	48.63±1.34[a]	9.53±0.22[a]	1.96±0.11[a]	111.56±1.35[a]
Smoker	82.15±2.92[b]	6.91±0.26[b]	0.82±0.1[b]	91.36±0.19[b]

Notes: [a, b] different letters refers to significant difference $p \leq 0.05$.

Table 4
Iron, calcium, magnesium and zinc according to the period of smoking (mean±SE)

Period (years)	Iron (µg/dL)	Calcium (mg/dL)	Magnesium (mg/dL)	Zinc (µg/dL)
1–15	78.44±2.51[a]	7.28±0.22[a]	0.9±0.1[a]	92.09±0.08[a]
16–30	93.28±1.91[b]	5.8±0.1[b]	0.56±0.07[b]	90.63±0.19[b]

Notes: [a, b] different letters refers to significant difference p≤0.05.

0.26 mg/dL). Magnesium in smoker women apparent significantly decline (0.82± 0.1 mg/dL) in compare with (1.96±0.11 mg/dL) in non-smoker. Similarly, Zinc was significantly decreased in smoker women (91.36±0.19 µg/dL) while in non-smoker was (111.56±1.35 µg/dL). Table 4 showed a significant increased (p≤0.05), in serum iron in the period of (16–30) year while the concentration of calcium, magnesium and zinc were significantly decrease in the period (16–30) in compare with (1–15) year.

■ DISCUSSION

Smoking cigarette was responsible for many dangerous diseases, such as anemia, cardiovascular disease, respiratory disorder, pancreatitis, diabetes mellitus and many type of cancer [11] and seem to cause changes in some haematological parameters [6].

Our result found that smoking effect hematological parameters, WBC, RBC, Hb, PCV, and MCV were higher in smoker women, these correlated with [20, 21]. The increase in hemoglobin concentration due to monoxide carbon exposure which bind together to form carboxy hemoglobin therefore the hemoglobin loses the capacity to carry oxygen [22]. Furthermore, increase cigarettes smoked per day and along time exposure to HbCO linked with polycythemia [23].

The increase in HCT and RBC can explained according to the role of carboxy hemoglobin which induce tissue hypoxia so increased erythropoietin hormone secretion which directly stimulate stem cell on red bone marrow to increase erythropoiesis [24], in the same time it cause increase in permeability of capillaries, lowering plasma volume and allow to rise RBC in blood that was reverse to HCT rise [25].

In our study the elevated of mcv may be indicate for any type of anemia independent in low folic acid, iron and vitamin B12 in the blood [7] or may due to changes in lipid and protein in the membrane of red blood cell because of enhance oxidative stress and free radicals as well as the toxic influence in bone marrow of acetaldehyde from smoking cigarette [23].

According to the period of smoking the results in table 2 found that the period (16–30) years of smoking was more effect on hematology indicator, the elevate in RBC and WBC count caused impairment in blood flow which enhance viscosity and clotting ability [26]. Concerning WBCs observed non-significant different between smoker women and non-smoker this result corresponding with the study [27] which find out higher level in WBCs in smoker women but not significant different with non-smoker women.

In the current study the results showed a significant rise in serum of iron in smoker women, this result is in agreement with other studies [28, 29]. Smoking cigarette induce low concentration of oxygen which stimulate increase in the secretion of erythropoietin [30] caused bone marrow hyperplasia which lead to secondary RBC development and

increase red cell mass count above normal level which cause increase in process of RBC production which in turn induce an increase in destruction of RBC lead to excess of iron in the bloodstream and accumulation in liver cell caused hepatocyte damage [31].

Furthermore, in the present study, serum Mg level was significantly decrease in smoker women. This is consistent with [32, 33] smoking cigarette cause decrease in appetite tend to less eat causing decrease of nutrient [34], also smoker suffering from digestive system disorder so reduce absorption of Mg [35], also the smoker demand for exhaustion more Mg to release a lot of adrenaline and rise the thermogenic effect of tobacco constituent predominately nicotine [33].

The results of our finding showed significant reduction in serum calcium among smoker women that is contradict with [36]. Researcher have found that nicotine cause disturbance in absorption of calcium in intestine via effect metabolism of calciotropic hormone and constriction or tighten the blood vessels [37]. Several researcher reported that smoking effect synthesis of steroid hormone and associated with deficiency of vitamin D either through disturbance of its metabolism and function or changing on genes responsible for the metabolism of vitamin D [38, 39], another researcher find that smoking women have reduction in PTH level compare to non-smoke [40] that due to effecting parathyroid gland cell, enhancing its degradation or the toxic effect of chemicals on tobacco which suppressed PTH secretion [41].

Significant difference in concentration of zinc was observed for smoker women compared with nonsmoker, the result confirm with [12, 26] the decrease in zinc probably independent to toxicity of tobacco components specifically in tar phase which contain heavy metals like cadmium, their action antagonistically to the action of Zn, therefore they competition on binding site in metallothionein the direct key for detoxification of cadmium [38, 42]. And because reduce absorption of zinc caused by tobacco chelation effect [12, 13] suggested that smoking induced hypozincemia through its effect on reduce the bioavailability of food intake in Duhok. Also, oxidative stress an important disorder related to smoking habit can influence of zinc metabolism [13].

■ CONCLUSION

Cigarette smoking causes health effects in women, including changes in blood parameters as leukocyte and erythrocyte count, Hb, hematocrit and MCV as well as the nutrients which necessary for body functions. Smoking is a risk factor for developing many dangerous diseases as atherosclerosis, polycythemia, pulmonary cancer and cardiovascular disease.

■ REFERENCES

1. Mathers M., Toumbourou J.W., Catalano R.F., Willims J., Patton G.C. Consequences of youth tobacco use: a review of prospective behavioural studies. *Addiction*. 2006;101(7):948–958.
2. *WHO Report on the Global Tobacco Epidemic, 2008: The MPOWER package.* Geneva: WHO; 2008. Available at: http://www.who.int/tobacco/mpower/mpower_report_full_2008.pdf
3. WHO. *Gender, Women and the Tobacco Epidemic: Addiction to Nicotine.* Available at: http://www.who.int/tobacco/pubications/gender/emn_tfi_gender_women_addiction_nicotine.pdf (accessed 2 January 2016).
4. Leifert J.A. International Journal of Laboratory Hematology. *Anemia and cigarette smoking*. 2008;30:177–184.
5. Syamlal G., Mazurek J.M., Dube S.R. Gender differences in smoking among U.S. working adults. *Am J Prev Med.* 2014;47(4):467–475. doi: 10.1016/j.amepre.2014.06.013
6. Asif M., Karim S., Umar Z., Malik A., Ismail T., Chaudhary A., Rasool M. Effect of cigarette smoking based on hematological parameters: comparison between male smokers and non-smokers. *Turk J Biochem.* 2013;38(1):75–80.

7. Malenica M., Prnjavorac B., Bego T., Dujic T., Semiz S., Skrbo S., Gusic A., Hadzic A., Causevic A. Effect of Cigarette Smoking on Haematological Parameters in Healthy Population. *MED ARCH.* 2017;71(2):132–136. doi: 10.5455/medarh.2017.71.132-136
8. Wannamethee S.G., Lowe G.D., Shaper A.G., Rumley A., Lennon L., Whincup P.H. Associations between cigarette smoking, pipe/cigar smoking, and smoking cessation, and haemostatic and inflammatory markers for cardiovascular disease. *Eur Heart J*. 2005;26(17):1765–1773.
9. Dass B.P., Jaganmohan P., Sravanakumar P. Changes in hematological and biochemical parameters in smokeless tobacco (ST) Chewers in Costal Belt of Andhra Pradesh, India. *European Journal of biological sciences.* 2013;5:29–33.
10. Mukherjee R., Chatterjee A. Assessment of the effects of smoking and consuming gutka (smokeless tobacco) on selected hematological and biochemical parameters: a study on healthy adult males of Hazaribag, Jharkhand. *International journal of pharmaceutical, chemical and biological sciences (IJPCBS).* 2013;3:1172–1178.
11. Alsalhen K.S., Abdalsalam R.D. Effect of cigarette smoking on liver functions: a comparative study conducted among smokers and nonsmokers male in El-beida City, Libya. *Inter Curr Pharm J.* 2014;3(7):291–295.
12. Al-Azzawy L.H.A., Al-Qaicy A.G.S. A study About Some Physiological Parameters In Smokers. *IBN AL-HAITHAM J. FOR PURE & APPL. SCI.* 2011;24(3).
13. AL-Timimi D.J., Haji M.R., Mohammad B.Y. Zinc status among smokers and non-smokers: relation to oxidative stress. *Duhok Medical Journal.* 2010;4(1).
14. Mudawi S., Ahmed S., AL-Abd. B. Assessment of the Levels of Serum Iron and Magnesium in Sudanese Cigarette Smokers. *IOSR Journal Of Pharmacy.* 2013;3(Issue 4):26–30.
15. Dhahir N.K., Noaman A.A. Study Effect of Cigarette Smoking on the Liver Functions and Electrolytes. *Iraqi Journal of Science.* 2017;58(1B):211–215.
16. Abou Turab M.K., Yser H.T. Environmental pollution adverse effects of smoking habits in smokers using cigarette and water pipe smokers volunteer. Basrah, Iraq. *Turkish Journal of Physiotherapy and Rehabilitation.* 2022;32(3):31171–31184.
17. Tietz N.W. *Text book of clinical chemistry. 3rd ed.* C.A. Burtis, E.R. Ashwood, W.B. Saunders. 1999:1698–1704.
18. Thomas L. *Clinical laboratory diagnostics 1st ed*. Frankfurt, TH-Books Verlagsgesellschaft, 1998:231–241.
19. Ray S.B.C., Chauhan U.P.S. *Anal Biochem.* 1967;20:155.
20. Lakshmi A.S., Lakshmanan A., Kumar G.P., Saravanan A. Effect of Intensity of Cigarette Smoking on Haematological and Lipid Parameters. *Journal of Clinical and Diagnostic Research.* 2014;8(7):11–3.
21. Nadia M.M., Shamseldein H.A., Sara A.S. Effects of Cigarette and Shisha Smoking on Hematological Parameters: An analytic case-control study. *International Multispeciality Journal of Health.* 2015;1(10):44–51.
22. Waseem S.M., Srivastava V.K., Bano R., Singh S., Dhunagana H. Anemia as co-morbidity in COPD: Comparative study of oxidant anti-oxidant imbalance in anemic and non-anemic COPD patients. *Int J Contemp Med Res.* 2017;4:1223–7.
23. Buckley C.M., Harrington J.M., O'Shea S., Perry I.J. Cigarette smoking is an under recognised cause of macrocytosis. *Blood.* 2013;122:4660.
24. Nunes A.R., Tata M. The impact of anaemia and iron deficiency in chronic obstructive pulmonary disease: A clinical overview. *Revista Portuguesa de Pneumologia.* 2017;23:146–155.
25. Verma R.J., Patel C.S. Effect of smoking on Haematological parameters in Human Beings. *Journal of Cell and Tissue Research.* 2015;5(1):337.
26. Ho C.H. White blood cell and platelet counts could affect whole blood viscosity. *J Chin Med Assoc.* 2004;67(8):394–397.
27. Arbab M., Batool Z., Afsheen H., Ali H., Naeem M., Tariq N., Hameed T., Tariq M.M., Bukhari F.A. Variation in hematological parameters in adult male and female smokers in Quetta city. *Pure and Applied Biology.* 2019;8(1):866–872.
28. Milnerowicz H., Wrzesniak M., Krolik M., Kowalska K. Influence of tobacco smoke on zinc, cadmium, iron, iron-binding proteins, and low-weight anti-oxidant status in pregnancy, Inhalation Toxicology. *International Forum for Respiratory Research.* 2018;30(13-14):534–541.
29. Abdullah E.S., Al-Shawi N.N. Estimation of serum levels of copper, zinc, and iron and cytological study of the impact of smoking on oral keratinocytes in a sample of tobacco smoke among Iraqi men. *Ann Trop Med & Public Health.* 2020;23(S19):SP232131.
30. Jelkmann W. Erythropoietin. *Front Horm Res.* 2016;47:115–27.
31. El-Zayadi A.R. Heavy smoking and liver. *World J Gastroenterol.* 2006;12:6098–6101.
32. Peacock J.M. Serum magnesium and risk of sudden cardiac death in the Atherosclerosis Risk in Communities (ARIC) Study. *Am Heart Journal.* 2010;160:464–70.
33. Khand F., Shaikh S.S., Ata M.A., Shaikh S.S. Evaluation of the effect of smoking on complete blood counts, serum C-reactive protein and magnesium levels in healthy adult male smokers. *J Pak Med Assoc.* 2015;65(1).
34. Kocyigit A., Erel D., Gur S. Effects of tobacco smoking on plasma selenium, zinc, copper, and iron concentrations and related antioxidative enzymes activities. *Clin Biochem.* 2021;34(8):629–33.
35. Winiarczyk A.U., Bagniuk A., Lalkowska K.G., Szubartowska E. Calcium, Magnesium, Iron, Zinc and Copper Concentration In the Hair of Tobacco Smokers. *Biol Trace Elem Res.* 2008;128:152–160.
36. Hussein S.E.O. Effect of Cigarettes Smoking on the Serum Levels of Calcium and Phosphate in Sudanese Males in Khartoum. *International Journal of Research in Pharmacy and Biosciences.* 2015;2(8):4–9.
37. Cusano N.E. Skeletal Effects of Smoking. *Current Osteoporosis Reports.* 2015;13(5):302–309.
38. Shi L., Nechuta S., Gao Y.T., Zheng Y., Dorjgochoo T., Wu J., Cai Q., Zheng W., Lu W., Shu X.O. Correlates of 25-hydroxyvitamin D among Chinese breast cancer patients. *PLoS One.* 2014;9(1):e86467. doi: 10.1371/journal.pone.0086467
39. Colao A., Muscogiuri G., Rubino M., Vuolo L., Pivonello C., Sabatino P., Pizzo M., Campanile G., Fittipaldi R., Lombardi G., Di Somma C. Hypovitaminosis D in adolescents living in the land of sun is correlated with incorrect life style: a survey study in Campania region. *Endocrine.* 2015;49(2):521–7. doi: 10.1007/s12020-014-0483-8
40. Fujiyoshi A., Polgreen L.E., Gross M.D., Reis J.P., Sidney S., David R., Jacobs D.R. Smoking habits and parathyroid hormone concentrations in young adults: The CARDIA study. *Bone Rep.* 2016;5:104–109. doi: 10.1016/j.bonr.2016.04.003
41. Jorde R., Saleh F., Figenschau Y., Kamycheva E., Haug E., Sundsfjord J. Serum parathyroid hormone (PTH) levels in smokers and non-smokers. The fifth Tromso study. *Eur. J. Endocrinol.* 2005;152:39–45.
42. Richter P., Faroon O., Pappas R.S. Cadmium and Cadmium/Zinc Ratios and Tobacco-Related Morbidities. *International journal of environmental research and public health.* 2017;14(10):1154.