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Smoking Habits and Their Association with Total Leukocytes Count among Healthy Men in Karachi, Pakistan

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Abstract: Cigarette smoking is associated with alterations in inflammatory markers among smokers. The present study was carried out to examine the association between smoking habits and total leukocytes count in a group of clinically healthy smokers. The study group consisted of 365 clinically healthy men, aged 20-60 years. Subjects were classified into different groups on the basis of their smoking habits and relationship between their smoking characteristics and total leukocytes count was investigated. Compared with nonsmokers, current smokers showed significantly high values of total leukocytes count ($P<0.001$). Among smokers total leukocytes count was found to be positively associated with intensity of smoking, pack-year and duration of smoking ($P<0.001$). Ex-smokers, even who had quit smoking for more than three years prior to the study, showed somewhat elevated levels of leukocytes count as compared to nonsmokers. These findings suggest a marked influence of smoking characteristics on increased leukocytes count which may persists long, even after smoking cessation.

Key words: Cigarette smoking · Smoking cessation · Total leukocytes count

INTRODUCTION

Cigarette smoking is a major risk factor for cardiovascular diseases (CVD) and the association of smoking with coronary heart disease, peripheral artery disease and stroke has been shown by a number of studies [1-3] On the other hand, giving up smoking has been reported to decrease the, risk of myocardial infarction and stroke [4]. Although the relationship between smoking and, cardiovascular diseases is well established, the underlying complex mechanism responsible remains largely elusive. Proposed potential mechanisms by which cigarette smoking increases the risk of CVD include haemostatic disturbance, lipid abnormalities and vascular endothelial dysfunction [5-7]. Inflammation is another possible mechanism responsible for the increased risk of CVD in smokers. Smoking has been reported to be associated with a variety of inflammatory markers such as C-reactive protein [8, 9], fibrinogen [10], albumins [11, 12], plasma viscosity and leukocytes [13, 14, 15]. Leukocytes are an essential element of inflammatory process [16] and independent predictor of coronary heart disease in smokers [17, 18]. Although some studies have reported leukocyte count increases with the number of cigarettes smoked daily and decreases after cessation of smoking [19, 20], data on smoking characteristics, such as duration of smoking, intensity of smoking, smoked pack-year, duration of abstinence from smoking and their association with leukocytes count is scanty. We therefore, investigated the association of smoking status (nonsmoker, ex-smoker, light smoker, moderate smoker and heavy smoker) and smoking characteristics (number of cigarettes smoked daily, pack-year and duration of smoking) with leukocytes count in a group of clinically healthy volunteers.

MATERIALS AND METHODS

Present study was carried out to investigate the relationship between smoking habits and total leukocytes count in a group of clinically healthy volunteers. The study group consisted of 365 volunteers in the age range

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20-60 years. The subjects were recruited from among hospital staff workers and patient's attendants from 20 different public and private hospitals of Karachi. Each subject gave an informed consent and study protocol was approved by the ethical review committee. Data on smoking habits and amount of tobacco consumed were collected by a self administered questionnaire to be filled in by the participant. The respondents who had a history of diabetes mellitus; history of ischemic heart disease or peripheral vascular disease; chronic renal disease; hypertension and use of non steroidal anti inflammatory drugs were excluded from the study. On the basis of smoking habits the subjects were divided into different categories. Nonsmokers were the respondents who affirmed that they have not smoked yet (or very rarely tried to smoke). Individuals who said that they currently smoke were defined as smokers and were categorized as light smokers (1-10 cigarettes/day), moderate smokers (11-20 cigarettes/day) and heavy smokers (more than 20 cigarettes/day). Cigarette pack-years were computed as duration of smoking (years) multiplied by the number of smoked cigarette divided by 20. Former smokers were those who had stopped smoking were categorized on the basis of the time they had stopped smoking prior to the study.

All the subjects were attended in the morning and a brief history of each subject was taken, along with measurement of height, weight and blood pressure on the study day. Blood pressure of each subject was measured with a mercury Sphygmomanometer and a standard stethoscope. Anthropometric measurements were carried out with the subjects wearing light clothes and no shoes. Body weight was measured by an electronic scale; height was measured by a fixed stadia rod. BMI was calculated as body weight (Kg) divided by body height (m) squared.

Each test procedure was carried out between 7-12 a.m. Subject rested in a sitting position for at least 20 minutes in a quiet room prior to blood sampling. Each blood samples was drawn from a large antecubital vein by means of a 18-G butterfly needle connected with a plastic syringe. A tourniquet was applied for the shortest time possible and released when the actual blood sampling began. 3 milliliters of blood was drawn and transferred into an EDTA tube for analysis using Coulter Model S-Plus IV within four hours of sample collection.

All the data was computed using statistical software package SPSS 12.0 (Chicago, IL. USA). The P values represent probability values for testing the simultaneous equality of the means and P values below 0.05 were considered to be statistically significant. Relative frequencies of the smoking status, medians and interquartile ranges of different smoking characteristics were calculated for different age groups. Baseline characteristics of the subjects were described as Mean ± SD. The values of leukocyte counts were presented as geometric means. Adjusted mean of leukocytes count for multiple confounding covariates such as BMI, systolic and diastolic blood pressure were computed according to smoking status and in quintiles of different smoking characteristics.

RESULTS

Table 1 shows baseline characteristics of 365 subjects. The Mean±SD age of subjects was 41.8±12.6 years. All the subjects were normotensive having mean systolic blood pressure 122±16 and mean diastolic blood pressure 82±10. Smoking status and relative frequencies of the subjects according to different age groups are shown in Table 2. Smoking was more common in the age groups below 40 years than in the age groups of above 40 years. The subjects had a tendency to start smoking in their teenage years. On average, subjects smoked 18.5 cigarettes daily and had a mean smoking history of 18.4 years (Table 3).

The association of smoking status and different characteristics of smoking with total leukocytes count is shown in table 4. After adjustment for age, BMI, systolic and diastolic blood pressures by multiple linear regression, total leukocytes count was positively associated with number of cigarette smoked, pack-years and duration of smoking. The mean total leukocytes count for nonsmokers was $6.4x10^9$/L. Among current smoking group total leukocytes count was $7.1x10^9$/L for light smokers, $7.6x10^9$/L for moderate smokers and $7.9x10^9$/L for heavy smokers, this rise in leukocytes count showed a substantial and consistent relationship between the number of cigarettes smoked daily and total leukocytes count. The mean difference in the

Table 1: Baseline characteristics of the subjects

Variable	Mean±SD	Range
Age (years)	41.8±12.6	20-65
BMI (Kg/m^2)	23.3±3.4	18-32
Systolic blood pressure (mmHg)	122±16	82-160
Diastolic blood pressure (mmHg)	82±10	40-120

Data expressed as Mean ± SD.

Table 2: Smoking status of subjects according to age groups

Age	Non-smokers (n=161)	Ex-smokers(n=35)	Light smokers(n=41)	Moderate smokers(n=53)	Heavy smokers(n=85)
20-29	51	7	12	10	24
30-39	44	10	18	21	30
40-49	35	7	5	10	10
50-60	31	11	6	12	21

Table 3: Distribution of smoking characteristics in the subjects *

Age	Cigarettes per day	Pack-year	Duration of smoking
20-29	15 (0-40)	9.15 (0-30.00)	13 (1-15)
30-39	25 (0-50)	26.40 (0-45.00)	17 (1-20)
40-49	20 (0-50)	20.15 (0-35.00)	23 (1-25)
50-60	18 (0-40)	14.45 (0-40.00)	28 (1-30)

* Data expressed as median (IQ-range)

Table 4: Distribution of leukocytes count according to smoking characteristic of subjects

Smoking characteristics	No. of subjects	Leukocytes count($x10^9$/L)	P value*
Smoking status			
Nonsmokers	161	6.4	
Ex-smokers (1-10 cig/daily)	35	6.7	
Light smokers (1-10 cig/daily)	41	7.1	<0.001
Moderate smokers (>20 cig/daily)	53	7.6	<0.001
Heavy smokers	85	7.9	<0.001
Cigarette pack-year			
0.0-1.4	12	6.8	
1.5-10.0	36	7.1	
11.1-20.0	31	7.4	
20.1-35.0	22	7.7	
35.1-120.5	78	7.9	<0.001
Duration of smoking			
0-10	34	6.8	
11-20	40	7.2	
21-30	56	7.8	
>20	49	7.9	<0.001
Years since quitting smoking			
<1	4	6.7	
1-2	7	6.7	
2-3	11	6.6	
>3	13	6.6	0.256

Means (adjusted for age, BMI, systolic and diastolic blood pressure) computed from normalized transformed values. * P values for testing the equality of the means.

leukocytes count was 1400 cells when heavy smokers compared with nonsmokers (P<0.001). Similarly a difference of 1000 cells was observed between those who were smoking for less than 10 years and more than 30 years (P<0.001). Ex-smokers, even those who had quit smoking more than three years prior to the study had slightly increased mean total leukocytes count as compared to nonsmokers ($6.6x10^9$/L vs $6.4x10^9$/L), but the difference was not statistically significant.

DISCUSSION

The results of present study demonstrate a strongly positive relationship between cigarette smoking and total leukocytes count in healthy current smokers. A crucial role of smoking in this change is supported by the dose dependent relationship, with a larger effect seen in heavier smokers; these results are in consistence with previous studies [21, 22].

The precise mechanism responsible for smoking associated elevated leukocytes count is unclear. Nicotine may produce smoking induced leukocytosis via circulating catecholamine, as an increase in certain endogenous hormones levels such as epinephrine and cortisol have been reported, which are both known to increase total leukocytes count [23]. An acute or chronic inflammatory response induced by particulates of cigarette smoke may also be another possible mechanism responsible for increased leukocytes count in smokers [16, 24]. Reports on differential counts associated with smoking have been inconsistent. Some studies report only an elevation of neutrophils [21], while other implicate lymphocytes [22], or a combination of neutrophils, lymphocytes and monocytes [25, 26]. A further clarification of these relationships may therefore help to explain the underlying mechanism.

Substances released by leukocytes, could be pathogenic in cancer, cardiovascular and pulmonary diseases [25, 27]. A quantitative relationship between leukocytes count and diseases among smokers has been reported in some studies. A decrease of 9-25% leukocytes count has been related to 14% decrease in the risk of cardiovascular diseases related deaths and a 10% increase in total leukocytes count has been related to a 6.3% increase in chronic cough and 8.9% increase in chronic bronchitis [28]. In the present study, increased leukocytes count among smokers is of a magnitude similar to the above mentioned associations which might forecast the possible high risk for developing fatal disease in this group of population.

Although decrease in leukocytes count after smoking cessation has been reported In previous studies [4, 19, 20, 29], interestingly, we found somewhat elevated leukocytes count in ex-smokers even after more than three years of quitting smoking. Since we did not bio-chemically verify their smoking cessation in this study, this group indeed might have been occasionally smoking; and if not, smoking induced increased leukocytes count may persist long after smoke exposure is terminated.

In conclusion, we found a strong and consistent association of increased leukocytes count with smoking and various smoking characteristics. The present finding supports the previous reports and may help us to understand the distribution of leukocytes count among different sub groups of smokers. A limitation of this study is, we relied exclusively on subjects "self reports of smoking cessation" rather than requiring biochemical validation of their smoking status. This may have made it difficult to interpret the result of smoking cessation on leukocytes count in present study. Therefore, it is suggested that when studying the effects of smoking cessation biochemically confirmed smoking status of the subjects should be ensured. The findings of the present study, together with previous reports confirm a marked influence of cigarette smoking on total leukocytes count, which may predict high risk for some fatal diseases in smokers. Furthermore, following smoking cessation, these elevated levels of leukocytes count may take many years before returning back to normal values.

REFERENCES

1. Ambrose, J.A. and S.R. Barua, 2004. The Pathophysiology of Cigarette Smoking and Cardiovascular Disease. J. Am. Coll. Cardiol., 3(10): 1731-37.
2. Fowkes, F.G., E. Housley and R.A. Riemersma, 1992. Smoking, lipids, glucose intolerance and blood pressure as risk factors for peripheral atherosclerosis compared with ischemic heart disease in the Edinburgh Artery Study. Am. J. Epidemiol., 135: 331-340.
3. Shinton, R. and G. Beevers, 1989. Meta-analysis of relation between cigarette smoking and stroke. Br Med. J., 298: 789-794.
4. Wannamethee, S.G., A.G. Shaper, P.H. Whincup, *et al.,* 1995. Smoking cessation and the risk of stroke in middle aged men. JAMA., 74: 155-160.
5. Meade, T.W., J. FImeson and Y. Stirling, 1987. Effects of changes in smoking and other characteristics on clotting factors and the risk of ischemic heart disease. Lancet, 2: 986-88.
6. Schefer, E., E. Wiest and J. Woehrle, 1992. Smoking influences the atherogenic potential of low density lipoprotein. Clin Invest., 70: 263-268.
7. Barua, R.S., J.A. Ambrose, D.C. Saha, *et al.,* 2002. Smoking is associated with altered endothelial derived fibrinolytic and antithrombotic factors: an in vitro demonstration. Circulation, 106: 905-908.
8. Crook, M.A., D.A. Scott and J.A. Stapleton, 2000. Circulating concentrations of C-reactive protein and total sialic acid in tobacco smokers remain unchanged following one year of validated smoking cessation. Eur. J. Clin. Invest., 30: 861-865.
9. Gram, J., E.M. Bladbjerg and L. Moller, 2000. Tissue-type plasminogen activator and C-reactive protein in acute coronary heart disease. A case-control study. J. Intern. Med., 247: 205-212.

10. Lowe, G.D.O., A. Rumley, J. Norrie, *et al.,* 2000. Blood rheology, cardiovascular risk factors and cardiovascular disease: the West of Scotland Coronary Prevention Study. Thromb Haemost., 84: 553-558.
11. Bermudez, E.A., N. Rifai, J.E. Buring, *et al.,* 2002. Relation between markers of systemic vascular inflammation and smoking in women. Am. J. Cardiol., 89: 1117-1119.
12. Bazzano, L.A., H. Jiang, P. Muntner, *et al.,* 2003. Relationship between cigarette smoking and novel risk factors for cardiovascular disease in the United States. Ann. Intern Med., 138: 891-97.
13. Bonithon-Kopp, C., J. Levenson and P.Y. Scarabin, 1993. Longitudinal associations between plasma viscosity and cardiovascular risk factors in a middle-aged French population. Atherosclerosis, 104: 173-182.
14. Hansen, L.K., R.H. Grimm and J.D. Neaton, 1990. The relationship of white blood cell count to other cardiovascular risk factors. Int. J. Epidemiol., 19: 881-888.
15. Danesh, J., R. Collins and P. Appleby, 1998. Association of fibrinogen, C-reactive protein, albumin or leukocyte count with coronary heart disease: meta-analyses of prospective studies. J. Am. Med. Assoc., 279: 1477-1482.
16. Frohlich, M., M. Sund, H. Lowel, *et al.,* 2003. Independent association of various smoking characteristics with markers of systemic inflammation in men: results from a representative sample of the general population (MONICA Augsburg Survey 1994/95). Eur. Heart. J., 24: 1365-1372.
17. Brown, D.W., W.H. Giles and J.B. Croft, 2001. White blood cells count an independent predictor of coronary heart disease mortality among a national cohort. J. Clin. Epidemiol., 54(3): 316-322.
18. Petitti, D.B. and H. Kipp, 1986. The Leukocyte count: Associations with intensity of smoking and persistence of effect after quitting. Am. J. Epidemiol., 123(1): 89-95.
19. Van Tiel, E., P.H. Peeters and H.A. Smit, 2002. Quitting smoking may restore hematological characteristics within five years. Ann. Epidemiol., 12(6): 378-88.
20. Abel, G.A., J.T. Hays, P.A. Decker, *et al.,* 2005. Effects of biochemically confirmed smoking cessation on white blood cell count. Mayo. Clin. Proc., 80(8): 1022-8.
21. Schwartz, J. and S.T. Weiss, 1994. Cigarette smoking and peripheral blood leukocyte differentials. Ann Epidemiol., 4: 236-242.
22. Yarnell, J.W.G., P.M. Sweetnam and S. Roger, 1987. Some long term effects of smoking on the haemostatic system: A report from the Caerphilly and Speedwell collaborative surveys. J. Clin. Pathol., 40: 909-913.
23. Kapoor, D. and T.H. Jones, 2005. Smoking and hormones in health and endocrine disorders. Eur. J. Endocrinol., 152(4): 491-499.
24. Ogawa, Y., M. Imaki and Y. Yoshida, 1998. An epidemiological study on the association between the total leukocyte and neutrophil counts and risk factors of ischemic heart disease by smoking status in Japanese factory workers. Appl. Human. Sci., 17: 239-247.
25. Corre, F., J. Lellouch, D. Schwartz, *et al.,* 1971. Smoking and leukocyte counts: Results of an epidemiological survey. Lancet, 2: 632-634.
26. Schwartz, J. and S.T. Weiss, 1993. Peripheral blood leukocyte count and respiratory symptoms. Ann Epidemiol., 3: 57-63.
27. Sparrow, D., R.J. Glynn, M. Cohen, *et al.,* 1984. The relationship of peripheral leukocyte count and cigarette smoking to pulmonary function among adult males. Chest, 86: 383-386.
28. Grimm, R.H., J.D. Neaton and W. Ludwig, 1985. Prognostic importance of the white blood cell count for coronary, cancer and all cause mortality. JAMA., 254(14): 1932-1937.
29. Otsuka, R., K. Tamakoshi and K. Wada, 2008. Having More Healthy Practice was Associated with Low White Blood Cell Counts in Middle-aged Japanese Male and Female Workers. Industrial Health, 46: 341-347.