Original Article

Estimation of Plasma Fibrinogen Level in Smokers and Non-Smokers and Its Correlation with Duration of Smoking: A Comparative Study

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ABSTRACT

Objective: The aim of present study is to estimate plasma fibrinogen level in smokers & non-smokers in order to provide and validate the evidence for high fibrinogen level in smokers as a risk factor for cardiovascular disease.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Govt. Lady Reading Hospital, Peshawar, from September 2016 to May 2017.

Materials and Methods: Subjects included 250 healthy male smokers and 250 healthy male non-smokers as control, selected randomly from general population of Peshawar. Smokers were divided into light, moderate & heavy smokers groups and also on the basis of duration of smoking. Fibrinogen level of whole sample was measured using coagulation analyzer Sysmex 530. The results were analyzed using SPSS 16.

Results: Out of 250 smokers, 94 (37.6%) were light smokers, 71 (28.4%) were moderate smokers and 85 (34%) were heavy smokers. 43 (17.2%) smokers were smoking for the last 5 years, 64 (25.6%) were smoking for 5 to 10 years and 143 (57.2%) were smokers for more than 10 years. Increased Fibrinogen level was noted with increasing intensity of smoking. Increased duration of smoking also increased the plasma fibrinogen in light and moderate smokers, while in heavy smokers smoking was the only dominant factor affecting the plasma fibrinogen.

Conclusion: Smoking was found to be a dominant determinant of plasma fibrinogen level in smokers who were otherwise healthy. The plasma fibrinogen was also found to be positively correlated with intensity and duration of smoking.

Key Words: Fibrinogen, smoking, cardiovascular disease.

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INTRODUCTION

Tobacco smoking is the inhalation of smoke from leaves of tobacco plant, usually in Cigarettes form[1]. Tobacco has been smoked in one form or another since 2000 BC. People often smoke, casually for pleasure, habitually to satisfy nicotine addiction or in response to social pressure[1].

Tobacco smoking is major health problem across the world and studies have shown direct relationship between smoking and different diseases e.g coronary artery disease(CAD), lung and bladder cancer, emphysema, neonatal mortality and peripheral vascular disease. Cigarette smoking is 1st modifiable and second major risk factor for cardiovascular disease e.g. aneurysms, coronary heart diseases (CHDs), stroke and peripheral vascular diseases [2].

Almost 50% of high risk of cardiovascular diseases in smokers is mediated through the effect of smoking on plasma fibrinogen which is raised in smokers as compared to non-smokers. Interlukein-6 level is increased by cigarette smoke in smokers by stimulation of macrophages in the lungs, which is mediated by increasing CD4O ligand (CD4OL) expression on platelets and CD4O expression on monocytes. Interleukein-6 when reaches liver, stimulates increased synthesis of fibrinogen by hepatocytes through inducing the binding of nuclear transcriptional factors to interleukein-6 responsive element of fibrinogen gene[3]. Fibrinogen formed in liver is an acute phase reactant later converted to fibrin[4]. Studies showed an important association between cardiovascular diseases and increased fibrinogen level. Plasma fibrinogen is also associated with the risk of COPD, its progression, and mortality even independent of other risk factors[5].

Recently, in addition to traditional risk factors for cardiovascular diseases a lot of attention has been paid to these newly identifiable risk factors for CVD whose presence may denote even greater risk than from

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summation of the traditional risk factor[6,7]. In men, incidence of Myocardial infarction (MI) is 6 times greater in those with high cholesterol and high fibrinogen level compared to those who had high cholesterol and low fibrinogen level[8,9].

The aim of our present study is to evaluate the plasma fibrinogen level in smokers in order to provide and validate the evidence for high fibrinogen level in smokers as a risk factor for cardiovascular disease in them, to compare fibrinogen levels among smokers and non-smokers and also to compare fibrinogen levels among smokers with respect to smoking status and duration.

MATERIALS AND METHODS

This cross sectional study was conducted at district Peshawar, from January 2017 to July 2017. Sample of 250 healthy male smokers as cases and 250 healthy male non-smokers as controls were taken. The smokers and controls were well matched according to age (Both the groups ranged from 25 years to 55 years of age). All these subjects were included on their own written informed consent after explaining the purpose of conducting this research.

An individual was labeled as smoker who smoked minimum of 5 cigarettes a day for at least past 5 years with no abstention from smoking in the past 1 to 2 weeks because abstention from smoking for a period of 1-2 weeks causes a significant fall in plasma fibrinogen level. On the other hand, the controls (non-smokers) were those individuals (in the same age group as smokers) who were neither active smokers (lifelong non-smokers), nor passive smokers. The smokers were divided into three different groups based on the number of cigarette they smoked per day viz. (i) Light smokers (who smoked 5 cigarettes per day) (ii) Moderate smokers (who smoked 6-10 cigarettes per day) and (iii) Heavy smokers (>10 cigarettes per day)[14,15]. Smokers were also divided in to three groups on the basis of duration of smoking as: (i) Those smoking for the last 5 years (ii) for 5-10 years and (iii) Those smoking for more than 10 years. Those subjects having any history of coagulation or bleeding disorder, history of cardiovascular disease diabetes, chronic chest, anyone with BMI more than 25 or having history of mental illness were excluded from the study. Moreover, subjects who have received blood transfusion within last four weeks or having history of using steroid or barbiturates and those who were ex-smokers were also excluded from the study.

The laboratory work of the study was conducted at the hematology section of Pathology department of Government Lady Reading Hospital, Peshawar. The fibrinogen level assessment was done applying Clauss principle and using coagulation analyzer Sysmex 530 and thrombin reagent. The results were analyzed using SPSS Version 16. Continuous numerical variables were presented as means ± SD. To check the significant differences between the means of healthy controls and that of smokers, independent two samples t-test was applied.

RESULTS

Out of 250 smokers, 94 (37.6%) were light smokers, 71 (28.4%) were moderate smokers and 85 (34%) were heavy smokers. 43 (17.2%) smokers were smoking for the last 5 years, 64 (25.6%) were smoking for more than 5 to 10 years and 143 (57.2%) were smokers for more than 10 years. Among those 43 smokers who were smoking for the last 5 years; 25 (58.1%) were light smokers; 10 (23.2%) were moderate smokers and 8 (18.6%) were heavy smokers. Among those 64 smokers who were smoking for 5-10 years; 26 (40.6%) were light smokers; 18 (28.1%) were moderate smokers and 20 (31.2%) were heavy smokers. Among those 143 (30.06%) smokers who were smoking for more than 10 years; 43(30.06%) were light smokers; 43 (30.06%) were moderate smokers and 57 (39.8%) were heavy smokers. The results are shown in Table No.1& Table No.2:

Table.No.1 Shows the comparison of mean plasma fibrinogen (mpf)level of light, moderate and heavy smokers withmpf level of controls . It was seen that the mpf level of light smokers,253.87 mg/dl ± 45.68 is significantly different from mpf level of controls,233.67mg/dl± 55.57 (p-value< .002) when compared. The mpf level of moderate smokers 316.71 mg/dl ± 57.51 was highly significantly different from mpf level of controls(p-value< .001)when compared .Similarly the mpf level of heavy smokers,407.45 mg/dl ± 80.12 was also highly significantly different from mpf level of controls showing a p-value of <0.001.

Table.No. 2 Shows comparison of mpf level of smokers of same smoking status among themselves regarding different duration since smoking, using t-test .It shows that among the light smokers ,when the mpf level of those smoking since 5 years(group 1),219.05 mg/dl ±36.73 were compared with mean fibrinogen level, 257.68 mg/dl ± 42.06 of those smoking since 5 to10years(group 2) ,the difference was highly significant(p-value<0.001).Similarly when the former group was compared with the mpf level,271 .48 mg/dl ±41.74 of group which was smoking since >10 years(group 3), again the difference was highly significant (p-value< 0.00 1).But when the mpf level of the those smoking since 5 to 10 years(group 2) was compared with the group smoking since >10 years(group 3) ,the difference was not significant(p-value<0. 192)

Among the moderate smokers, when the plasma fibrinogen level 269.7 1 mg/dl ±48.28 of (group 1) was compared with the mpf level, 295.52 mg/dl ± 52.02 of (group 2) ,the difference was found not to be

significant(p-value< 0.209).The comparison of former group with the mean fibrinogen level, 336.29 mg/dl ±52.98 of (group 3), however, showed significant difference(p-value< 0.00 1).Similarly when the plasma fibrinogen level of (group 2) was compared with (group 3) ,the difference was highly significant(p-value< 0.00 8)

Among the heavy smokers ,the comparison of mpf level 395.22 mg/dl ± 82.99 of (group 1) with mean fibrinogen level 400.22 mg/dl ± 81.25 of (group 2) showed non significant difference(p-value< 0.88).Similarly when the former group was compared with mpf level 411.70 mg/dl ± 80.44 of(group 3),the difference was non significant(p-value< 0.591).There was also non significant difference (p-value< 0.586) between the group 2 & group 3 in the mpf level.

Table No. 1: Comparison of mean plasma fibrinogen level in smokers and control

Smoking status	Smokers		Controls		*t*-ratio	P-value
	Mean	SD^{+}	Mean	SD		
Light	253.87 (94)	45.68	233.67 (250)	55.57	3.147**	<0.002
Moderate	316.71 (71)	57.51	233.67 (250)	55.57	1l.026**	<0.001
Heavy	407.45 (85)	80.12	233.67 (250)	55.57	2.208**	<0.001

The values in brackets are the number of respondents in a group; SD represents standard deviation; ** significant at 1 % level of significance

Table No. 2: Comparison of Mean Plasma Fibrinogen Level In Different Groups of Smokers of Same Smoking Status With Respect To Duration of Smoking

Light Smokers							
Group	Mean	SD	Group	Mean	SD	*t*-ratio	p-value
1	219.05(25)	36.73	2	257.68(25)	42.06	-3.458**	<0.00 1
1	219.05(25)	36.73	3	271.48(44)	41.74	-5.23 **	<0.001
2	257.68(25)	42.06	3	271.48(44)	41.74	1317 ^{NS}	<0.192
Moderate Smokers							
1	269.71(10)	48.28	2	295.52(18)	52.02	- l.290^{NS}	<0.209
1	269.71(10)	48.28	3	336.29(43)	52.98	- 3.63**	<0.001
2	295.52(18)	52.02	3	336.29(43)	52.98	- 2.755**	<0.008
Heavy smokers							
1	395.22(8)	82.99	2	400.22(20)	81.25	-0.146^{NS}	<0.88
1	395.22(8)	82.99	3	411.70(57)	80.44	-0.4l ^{NS}	<0.591
2	400.22(20)	81.25	3	411.70(57)	80.44	0547^{NS}	<0.586

Shows the number of respondents in the corresponding group. SD sand for standard deviation ** indicates significant at 1% level of significance; NS stands for non significant. 1, 2 and 3 denotes the duration groups (5 years), (5-l0 years) and (>l0 years)

DISCUSSION

The present study was aimed to identify and confirm one of the most important risk factor i.e. high fibrinogen level in smokers of our population. In this cross section population based study, we were able to demonstrate dose effect of fibrinogen from cigarette smoking and also its correlation with duration of smoking.

In a study, almost 50% of cardiovascular risk attributable to smoking was mediated through an increase in fibrinogen level requiring the need for such studies to identify and validate the role of high fibrinogen level in smokers of general population[10-12]. A study was conducted in Dow Medical College Karachi. This study compared the patients with ischemic heart disease to the healthy controls. Patients were sub grouped into smokers and non-smokers and the results showed that fibrinogen levels of smokers differed significantly from non-smoking healthy controls as well as non-smoker patients[13,14]. Another previous study conducted on smokers' fibrinogen level, in which smokers were divided into light and heavier smokers; fibrinogen levels were found higher in heavier smokers as compared to lighter smokers[15].

We compared our results to all these studies and found that the result of present study are exactly consistent with these previous studies, showing that fibrinogen levels are consistently higher in all three categories of smokers as compared to non-smokers showing a P-value <0.002, 0.001 and 0.001 in light, moderate and heavy smokers respectively as compared to non-smokers control. Also in our study, when light smokers were compared to moderate and heavy; the difference found in mean plasma fibrinogen level was highly significant (p-value 0.001) in both. Similarly comparison of moderate smokers to heavy smokers with regard to the mean fibrinogen level also showed highly significant difference (p-value 0.00 1) which is consistent with previous studies i.e showing positive relation of fibrinogen level to the increasing number of cigarettes

smoked. These findings are consistent with the study done by Robert.S. Rosenson in 2005[16].

The present investigation shows that difference in duration since smoking doesn't influence mean plasma fibrinogen level except in light smokers where comparison of mean fibrinogen level of subjects smoking since 5 years showed significant difference when compared with fibrinogen level of subjects smoking for 5-10 years and to subjects smoking since >10 years. It also shows variable results in three categories of smoking status with respect to duration since smoking. Among light smokers, comparison of mean fibrinogen level of subjects smoking since 5 years to mean fibrinogen of subjects smoking for >5-10 years showed significant difference. Similarly comparison of mean fibrinogen level of subjects smoking for 5 years and subjects having history of smoking since>10 years also showed significant difference. However, comparison of smokers with habit extending over 5 to 10 years with the ones with>10 years history showed no significant difference. The reason might be that most probably the 5 years duration is not too much to influence the fibrinogen level. While the 10 years duration is enough to affect fibrinogen level even within the same smoking status.

Among the heavy smokers, none of the duration differed from other significantly probably because with heavy smoking, the intensity of smoking is dominant factor determining the fibrinogen level, irrespective of duration of smoking. So in this respect our study is exactly consistent with the previous studies where they found duration not to be associated positively to fibrinogen if the smoking intensity is the same[15]. The ultimate conclusion of duration comparison in our study shows that duration does affect the fibrinogen level in light and moderate smokers to some extent but there is no effect of duration since smoking upon fibrinogen level in heavy smokers group.

CONCLUSION

On the basis of present study, we conclude that among the smokers the concentration of fibrinogen increases as the intensity & duration of smoking increases thus reflecting the high risk of cardiovascular disease in heavy smokers as compared to moderate smokers and more risk in moderate as compared to light smokers.

Author's Contribution:

Concept & Design of Study:	Naila Aslam & Muhammad Khalid
Drafting:	Farhat Rehman & Fazal Rahim
Data Analysis:	Farhat Rehman & Fazal Rahim
Revisiting Critically:	Naila Aslam & Muhammad Khalid
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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