The effect and correlation of pack years of smoking on the hematological parameters, lipid profile and coagulation profile: A case control study

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Abstract: *Introduction:* Cigarette smoking is considered a major risk factor for atherosclerosis, coronary heart disease, stroke and cancer. *Objectives:* To compare the Complete Blood Count, Lipid Profile and Coagulation profile (PT, aPTT) in the smokers and non-smokers and to study the correlation of pack years of smoking with the above parameters. *Methodology:* The study was a case control study (110 smokers as cases and 110 non smokers as controls). The cases were grouped into mild smokers (<5 pack years), moderate smokers (5-10 pack years) and heavy smokers (>10 pack years).A complete blood count including Differential leucocyte count, Lipid Profile and Coagulation profile was done. *Observation and Results:* The RBC count and TLC were significantly elevated, however, MCV and MCH were significantly reduced in the smokers with a p value <.05. The S. cholesterol and LDL values were raised in the smokers (168.58±39.95 versus 157.71±35.94) and (103.92±35.01 versus 93.86±29.76) respectively. A significant difference was found in the TLC, S. cholesterol and S. Triglyceride values among the mild, moderate and severe smokers with p values 0.023, 0.022, 0.014 respectively. A significant positive correlation of pack years of smoking with TLC, S. Cholesterol, S. triglyceride and a PTT was also noted with correlation coefficients 0.320 (p = 0.023) ,0.21(p=0.027), 0.230(0.015) and 0.379 (p= 0.0004) respectively. *Conclusion:*A significantly increased RBC count and TLC, however reduced MCV and MCH was noted in smokers. Also the smokers were associated with a significant positive correlation of S. Chol, S. TG with increasing pack years of smoking. The coagulation profile (aPTT) was also affected in the smokers with a strong positive correlation with increasing pack years of smoking. Thus the monitoring of the hematological parameters like TLC, RBC and lipid profile (S. Chol and S.TG) and aPTT would help in early intervention and thus reducing the morbidity and mortality due to smoking.

Keywords: aPTT, MCV, MCH, RBC count, S. Cholesterol, S. Triglyceride.

Introduction

Cigarette smoking is a major public health concern and tobacco use is the single most significant cause of preventable death worldwide [1]. The World Health Organization (WHO) predicts that by the year 2020 the tobacco related deaths may exceed 1.5 million annually [2]. Cigarette smoking is considered a major risk factor for atherosclerosis, coronary heart disease, stroke, cancer and has relationship with gastric ulcer, periodontal disease, sudden infant death syndrome and metabolic syndrome [3-5]. Smoking has severe adverse effects like intense hematological changes, initiation of endothelial injury, acceleration of coronary progression, new lesion formation and overall alterations in lipid and hemostatic systems [6-7].

Nicotine induces hypercoagulability and hyperthrombosis due to increased platelet aggregation and adhesiveness and also stimulates hormone secretion that leads to increase in total leucocyte count [8]. Inflammation is another possible mechanism for the increased cardiovascular risk in smokers. Leucocytes are an essential element of inflammatory process and independent predictor of coronary heart disease and stroke in smokers [9-10].

Studies revealed that oxidative stress from cigarette smoke impairs the function of liver cells which include production of some coagulation factors. Nicotine induced oxidative stress affects intrinsic pathway of coagulation producing hypercoagulable state in smokers [11]. Smoking reduces the distensibility of blood vessel walls, and induces impairment of lipoprotein metabolism, pro-thrombotic and pro-inflammatory state [12].

The changes in extensive hematological parameters, coagulation and lipid profile due to varying intensity and duration of cigarette smoking have been sparsely studied. Thus, the aim of this study was to analyze the effects and assess the correlation of pack years of smoking with the hematological (complete blood count and differential leukocyte count) as well as Lipid profile (S. chol, S. TG, LDL and VLDL) and coagulation profile (PT and aPTT).

Material and Methods

The study was conducted in a tertiary care hospital within a period of two months (July 2019 to August 2019).A total of 220 cases, 110 controls and 110 cases of smokers which were grouped according into Mild (pack years <5), Moderate (pack Years 5-10) and Heavy Smokers (pack years >10). Individuals with associated co-morbid illness, hematological disorder, and family history of lipid disorders or taking antioxidants were excluded from the study.

Under aseptic conditions 8mL venous sample was collected and distributed in EDTA vial, plain vial and sodium citrate vial for analysis of CBC, serum for lipid profile and Prothrombin Time (PT) and activated Partial Thromboplastin Time (aPTT) respectively. All the CBC parameters including DLC, Lipid profile (Total cholesterol, HDL, LDL) and coagulation profile (PT, aPTT) were noted both for the cases and controls. A comparison was done among the smokers and non-smokers and also the effect of intensity and duration of smoking on the above mentioned parameters was studied.

Statistical Analysis: Appropriate statistical analysis using SPSS software was done including the t-test for comparison among the smokers and non-smokers and the effect of intensity and duration of smoking on the above parameters was

analysed using ANOVA tests and calculation of correlation coefficient(r) was done. A p-value <.05 was considered significant. Ethical clearance was taken from the institutional ethical committee *(Ethical Committee Approval:* 134/A/11/16/Academics/MC/2016/ 118 dt: 25.04.2019).

Results

The study included individuals in the age group ranging from 19-74 years. Of the 110 cases, 26 were heavy smokers with pack years >10, 27 were moderate smokers with pack years 10-15 and the rest 56 were mild smokers with pack year less than 5. Out of 110 smokers, 7 were females and the rest 103 were males (Figure 1).

Fig-1: Distribution of smokers according to pack years
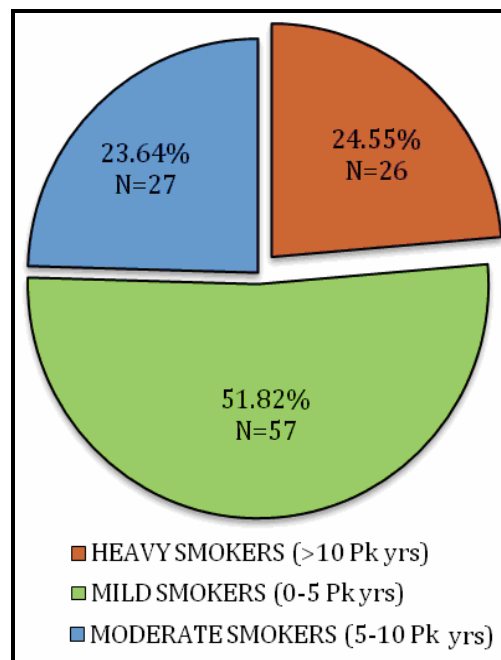
In the complete blood count, we found a significant difference in the RBC count, MCV and MCH with a p value <.05 in the cases and controls (Table 1). The Hb and hematocrit though not statistically significant had a higher value in the smokers (Table 1). Similarly TLC was higher in smokers with a mean value of 7558.54 ± 2130.65 in comparison to the non smoking group with a mean value of 6758 ± 1909.95 with a p value 0.003which was statistically significant(Table 1).

Table-1: Comparison of parameters between smokers and non-smokers			
Parameter	**Smokers (n=110)**	**Non-Smokers (n=110)**	**p value**
Hb (g/dl)	13.05±2.01	12.99±2.18	0.85
TLC (/uL)	7558.54±2130.65	6758 +_ 1909.95	0.003*
Neutrophils (%)	59.49±10.36	58.46±11.54	0.317
Lymphocytes (%)	28.12±9.11	28.5±9.84	0.931
Monocytes (%)	8.51±3.25	8.16±2.81	0.379
Eosinophils (%)	4.29±6.12	4.73±5.20	0.556
Basophils (%)	0.14±0.13	0.14±0.14	0.568
Hematocrit (%)	40.50±6.13	40.45±5.49	0.939
MCV (%)	90.92±9.33	87.04±8.86	0.001*
MCH (%)	29.37±3.77	28.12±4.01	0.016*
MCHC (%)	32.27±1.56	32.15±2.48	0.641
RBC (10^6/uL)	4.48±0.65	4.82±0.83	0.001*
PT	14.25±2.76	13.99±1.79	0.428
aPTT	29.67±3.71	30.17±3.76	0.471
S Cholesterol (Total) (mg/dl)	168.58±39.95	157.71±35.94	0.0321*
S Triglyceride (mg/dl)	136.07±61.10	126.05±60.39	0.222
HDL (mg/dl)	39.49±7.76	38.64±10.16	0.222
LDL (mg/dl)	103.92±35.01	93.86±29.76	0.022*
VLDL (mg/dl)	27.05±12.19	25.21±12.08	0.261

Table-2: Comparison of parameters between smoker groups				
Parameter	**Mild Smoker (<5 pack years)**	**Moderate Smokers (5-10 pack years)**	**Heavy smokers (>10 pack years)**	**p value**
Hb (g/dl)	13.24±1.96	12.9±2.34	12.63±1.96	0.925
TLC (/uL)	6695.±1642.25	7664.64±2508.08	8988.30±1856.67	0.023*
Neutrophils (%)	58.09±9.68	58.31±12.99	62.21±8.65	0.214
Lymphocytes (%)	29.61±8.29	28.63±17.74	25.75±7.46	0.193
Monocytes (%)	8.57±3.60	9.88±4.93	7.84±2.29	0.13
Eosinophils (%)	3.88±4.36	5.65±10.39	4.05±3.14	0.446
Basophils (%)	0.14±0.12	0.15±0.13	0.14±0.16	0.929
Hematocrit (%)	41.16±5.27	39.9±5.91	39.09±5.06	0.236
MCV (%)	90.55±7.91	92.68±6.78	90.17±13.39	0.555
MCH (%)	29.20±3.34	29.95±2.6	29.18±5.39	0.667
MCHC (%)	32.25±1.53	32.31±1.16	32.21±1.95	0.976
RBC (10^6/uL)	4.56±0.58	4.33±0.69	4.4±0.70	0.258
S Cholesterol (Total) (mg/dl)	161.58±39.32	158.15±38.13	182.56±38.55	0.022*
S Triglyceride (mg/dl)	127.57±57.78	110.77±36.78	157.92±67.13	0.014*
HDL (mg/dl)	39.67±7.73	40.18±8.54	37.63±6.63	0.42
LDL (mg/dl)	101.95±34.13	100.02 ±33.22	108.19 ±37.29	0.44
VLDL (mg/dl)	25.72±10.99	26.81±13.26	33.26±21.02	0.0851
PT	13.98±0.95	14.98±5.05	14.11±2.2	0.392
aPTT	29±1.94	29.1±3.25	30.46±5.18	0.133

A significant difference in TLC was found among the 3 group of smokers with Mean ± SD value of TLC in Mild Smokers as 6695 ± 1642.25, in Moderate Smokers7664 ± 2508.08 and Heavy Smokers 8988 ± 1856.67 and the difference was statistically significant (p=0.023)(table 2;Figure 2).Also we found a significant positive correlation between TLC and increasing pack years with correlation coefficient 'r' as 0.320 and p value =0.0006(HS) (table 3)(fig 3).

Fig-2: Graphical Representation of Total Lymphocyte Count (/uL) of Mild, Moderate and Heavy Smokers
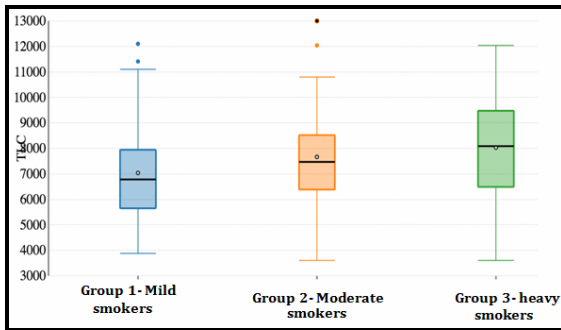
Fig-3: Correlation of pack years of smoking with TLC.(u/l)
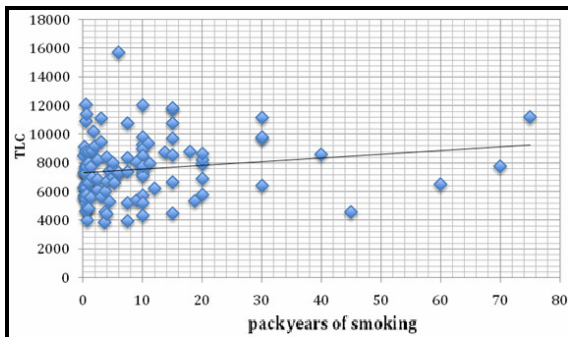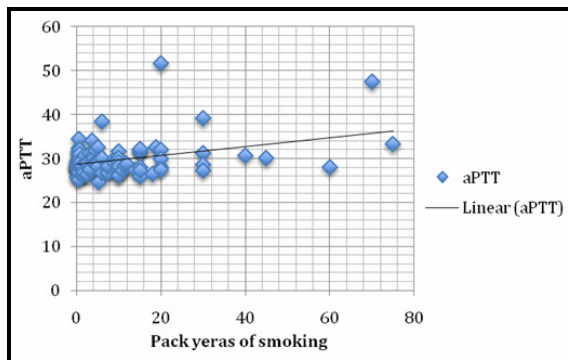

Fig-4: Correlation of pack years of smoking with aPTT

The mean value of PT and aPTT was slightly prolonged in smokers than control group

(14.25±2.76 v/s 13.99±1.79) and (29.67±3.71 vs 30.17±3.76) respectively (Table 1). However, the value of aPTT was significantly raised as the number of pack years increased with a correlation coefficient as 0.379 and p value as 0.0004(table 3) (fig4).

Table-3:Correlation of parameters with pack years		
Parameter	**Correlation coefficient 'r'**	**p value**
Hb (g/dl)	0.046	0.633
TLC (/uL)	0.320	0.0006*
Neutrophils (%)	0.18	0.058
Lymphocytes (%)	0.17	0.075
Monocytes (%)	0.059	0.540
Eosinophils (%)	0.044	0.640
Hematocrit (%)	0.080	0.406
MCV (%)	0.049	0.656
MCH (%)	0.012	0.900
MCHC (%)	0.053	0.582
RBC (10^6/uL)	0.013	0.892
S Cholesterol (Total) (mg/dl)	0.21	0.027*
S Triglyceride (mg/dl)	0.230	0.015*
HDL (mg/dl)	0.102	0.288
LDL (mg/dl)	0.158	0.099
VLDL (mg/dl)	0.0523	0.587
PT	0.006	0.954
aPTT	0.379	0.00004**

The lipid profile showed a significant increase in the cholesterol level and LDL level in the smokers as compared to non-smokers with a p value of 0.032 and 0.022 respectively(table 1). The TG and VLDL were increased in the smokers with a mean value of 136 ± 61.10 and 27±12.18 as compared to the nonsmokers with a mean value of 126 ± 60.39 and 25 ± 12.07 respectively (Table 1).

Among the three groups of smokers a significant difference with a p value of 0.022 and 0.014 was found in S. cholesterol and S. triglyceride levels respectively (table 2). We also found a significant positive correlation of S. cholesterol (fig- 5) and TG (fig -6) with

increasing number of pack years of smoking with a correlation coefficient of 0.210 (p value-0.027) and 0.230 (p value-0.015) (table 3).

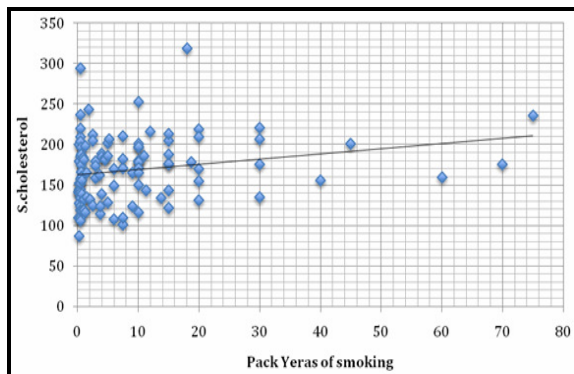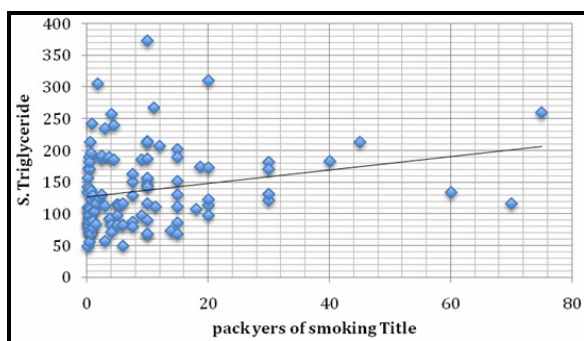**Fig-5:** Correlation of pack years of smoking with S. Cholesterol (mg/dl)

Fig-6: Correlation of pack years of smoking with S. Triglyceride (mg/dl)

Discussion

In the present study, a comparison of the hematological parameters, lipid profile and coagulation profile was done among the smokers and nonsmokers and also among the three groups of smokers (<5 pack years, 5-10 pack years and >10 pack years).Among the hematological parameters we found a significant increase in the RBC count, MCV and MCH in the smokers (Table 1). We also found that the Hb and HCT levels were higher in the smoker group; however a statistical significance could not be established. Lakshmi et al have reported a significant increase in the Hb and HCT levels in smokers and the RBC count increased with the intensity of smoking [2].

Whitehead et al also noted a significant increase in the hemoglobin concentration and hematocrit in smokers who were smoking more than 10

cigarettes per day [13]. Similarly Asif et al also reported significant increase in Hb, HCT and RBC count[15]. Melenica M et al noted a significant increase in MCH and MCV in the smokers; however MCHC was not significant which is consistent with our findings[14].

However, according to Asif et al MCHC was significantly increased in smokers, however nostatistically significant difference was found in MCV and MCH [15]. The CO is released from cigarette smoking which combines with Hb to form carboxyhemoglobin causing tissue hypoxia and functional anemia and release of erythropoietin leading to polycythemia and other changes in the hematological parameters [2, 16].

TLC was found to be significantly raised in smokers according to several authors which was consistent with our findings [14-15, 17]. A comparison of three groups of smokers (mild, moderate and heavy) showed a significant increase with a p value <.05 in the TLC, with the highest count being in the group of Pack years >10. The higher WBC count in smokers may be attributed to the release of catecholamines induced by nicotine and the inflammation of respiratory tree due to the irritant effect of cigarette smoke [2].

In the present study no significant difference was found in the coagulation profile (PT and aPTT) of smokers and non-smokers, however PT was marginally increased in the smokers as compared to control group. We also reported a significant positive correlation with increasing pack years of smoking with aPTT. Some researchers report prolonged PT and APTT in smokers [16, 18] while some authors report shorter PT and APTT or no significant correlation. [19-21].

Studies revealed that oxidative stress from cigarette smoke impairs the function of liver cell which include production of some coagulation factors. Nicotine induced oxidative stress affects intrinsic pathway of coagulation thus producing hypercoagulable state in smokers [11]. Smoking is associated with a more atherogenic lipid profile [5]. Total cholesterol and LDL was significantly

higher in the smokers as compared to nonsmokers, whereas other parameters (TG, HDL and VLDL) of the lipid profile did not show a significant difference in our study. Meenakshi Sundaram R et al reported a significant increase in TC, LDL, TG and Apo-B than control non-smoker group [5].

Similar findings were also reported by Anandhalakshmi et al [22] that included worsening of the lipid profile with increased intensity and duration of smoking, which is also noticed in our study where there was a significant difference in S. cholesterol and S. TG levels among the three smoker groups. However, we found a slight dip in the mean values in moderate smoker group as compared to mild smokers but the mean values were highly increased in the heavy smoker group. There was also a significant positive correlation of pack years of smoking with S. cholesterol and TG levels in our study. Smoking induced lipid alterations are linked to Nicotine induced secretion of hepatic free fatty acids, triglycerides and VLDL-C in blood stream by increasing the secretion of catecholamines and thus stimulating sympathetic adrenal system resulting in increased lipolysis [23]. Cigarette smoking is known to be associated with raised plasma Homocysteine level which causes oxidative modification of LDL-C and decreases HDL-C by inhibiting Apo A-I protein expression [24].

Conclusion

The present study demonstrated significant rise of TLC, RBC count in the smokers, however reduced MCV and MCH in the smokers. The S. Cholesterol and LDL were also significantly elevated in the smokers. There was a significant difference in the TLC, S. chol, TG, LDL and aPTT values among the mild, moderate and severe smokers. A positive correlation of TLC, S.chol, TG and aPTT with increasing number of pack years of smoking was also noted. Thus the monitoring of hematological parameters like TLC and RBC along with Lipid profile (S. chol, S. TG) and coagulation parameters (aPTT) which are easily available and inexpensive would help in predicting the morbidity in smokers and thus timely intervention can be done to prevent thromboembolic disorders and cardiovascular events.

Conflicts of interest: There are no conflicts of interest.

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