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Research Article

Assessment of Plasma Fibrinogen Level and Lipid Profile in Sudanese Smokers

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Abstract

Background: Cigarette smoking is a leading preventable risk factor for the development and progression of cardiovascular diseases (CVDs). Epidemiologic studies in smokers confirm the association between the alteration in lipid profile levels and CVDs risk. Fibrinogen, an acute phase reactant with active involvement in endothelial function, thrombosis and inflammation. It is signified as a systemic marker of carotid atherosclerosis. The purpose of this study was to assess the level of fibrinogen and lipid parameters in Sudanese tobacco smokers.

Methods: This case-control study included 55 adult male of a current smoking status; their ages ranged between 18 and 54 years, and 100 non-smokers considered as controls. We evaluated the effect of cigarette smoking on plasma fibrinogen and serum lipid profile. The American Heart Association guidelines and reference ranges were used to identify the smokers with increased risk of coronary heart disease.

Results: Our study revealed an increase in the levels of fibrinogen, total cholesterol, and low-density lipoprotein cholesterol (LDL-C) among smokers than controls, whereas the mean level of and triglycerides did not differ. The levels of high-density lipoprotein cholesterol HDL-C demonstrated decrement. Further, smokers were classified according to the atherogenic risk index LDL-C/HDL-C ratio, the studied parameters fibrinogen, total cholesterol, and triglycerides were significantly increased in those who have ratio 4.5 and more (p = 0.001, p = 0.018, p = 0.007, respectively). Smokers with atherogenic index ≥ 4.5 were more likely to have ≥ 300 mg/dl fibrinogen level (odds ratio (OR) 3.96, 95% confidence interval (95%CI) 1.14–13.73, p = 0.026). Moreover, the level of the fibrinogen can be predicted by linear regression equation: Fibrinogen level = 19.49 + 79.08 (the ratio of LDL-C /HDL-C), r = 0.37, p = 0.008, 95%CI 21.20–136.95. **Conclusion:** Increased fibrinogen, LDL-C, and LDL-C/HDL-C ratio may potentiate the development of cardiovascular disease in smokers.

Keywords: fibrinogen, lipid profile, smokers

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1. Introduction

The tobacco epidemic is one of the biggest public health threats the world affronted, killing around 6 million people a year. More than 5 millions of those deaths are the result of direct tobacco use. Nearly 80% of the more than 1 billion smokers worldwide live in low- and middle-income countries with increased risk to cardiovascular diseases (CVDs) [1, 2]. Smoking is estimated to cause nearly 10% of CVDs. The risk of CVDs mortality for persons who smoke cigarettes is about double that of lifetime non-smokers [3]. Disease risk due to smoking is not limited to smokers only, passive smoking, exposure to environmental tobacco smoke, is associated with adverse health effects, and it increases the risk of several diseases [4]. The smokers and passive smokers have a different lifestyle than non-smokers, as these people consume more calories, fat, and alcohol, and less fibre, fruit, vegetables, vitamin supplements, and useful oilseeds, which increase the incidence of atherosclerosis and coronary artery diseases in smokers [5].

Several studies confirm that smoking increases the level of inflammatory markers in blood as white blood cell count, fibrinogen, and C-reactive protein [6, 7]. Smokers have high-level total cholesterol (TC) and LDL cholesterol (LDL-C) levels and lower HDL cholesterol (HDL-C) levels exacerbating the risk of myocardial infarction, sudden cardiac death, stroke, peripheral vascular disease [8]. Most of the proposed proatherogenic actions of smoking, such as interference with blood coagulation, induction of endothelial dysfunction, and promotion of lipid per oxidation, reverse themselves shortly after cessation of smoking [9].

Fibrinogen is a plasma glycoprotein produced by hepatocytes in response to interlukin-1, interleukin-6, and tumour necrosis-α during acute severe infections [10, 11]. There is growing evidence from prospective studies that a higher plasma fibrinogen concentration is associated with increased risk, incidence, and severity of coronary heart disease [12–14]. Various studies suggested association between smoking status and elevated fibrinogen levels [15–18]. The purpose of this study was to assess the level of fibrinogen and lipid profile parameters in Sudanese tobacco smokers.

2. Materials and Methods

2.1. Study design and study subjects

The present study has been approved by the Faculty of Medicine, University of Gezira Ethics Committee. Furthermore, all smokers signed the formal consent before data and sample collection. This case-control recruited 55 male cigarettes smokers and 100 age–sex-matched non-smokers. All of them were from the Gezira state – Wad-Medani city, Sudan. A questionnaire was designed to collect personal information, clinical data, and smoking history from each participant. The study participants were clinically evaluated for their health, none of the participant reported to have diseases/disorders or medications that affect fibrinogen level or lipid parameters.

Blood samples were collected from participants in sodium citrate to measure plasma fibrinogen, and plain container for serum lipid profile estimation. All the blood samples were centrifuged at 3000rpm for 5 min at the room temperature and plasma lipid profile with fibrinogen were measured immediately. Automated analyzer accent-200 was used to estimate plasma fibrinogen by immuno-turbidimetric assay; and lipid profile by enzymatic spectrophotometric method.

2.2. Statistical analysis

Statistical analysis was carried out using Statistical Package for Sciences (SPSS, version 20). Data were expressed as mean ± standard error of mean (SEM) and compared firstly with controls and secondly with the provided reference values of the reagents and the data published in the literature. The smokers were stratified according to the atherogenic index (LDL-C/HDL-C) into two groups, group I (less than 4.5) and group II (4.5 and more), means of continuous variables were compared between the two groups using *t*-test. Then, the logistic regression analysis was performed to measure the risk estimate by odds ratio, 95% confidence intervals (95%CI), and *p*-value of having high concentrations of fibrinogen level in the two atherogenic groups. Besides, the linear regression test was applied to predict the level of fibrinogen in smokers using the atherogenic index.

3. Results

3.1. The general characteristics of the study group and the comparison of the measured parameters

Smokers' ages ranged between 18 and 54 years with the mean age of 27.60 ± 0.95. The mean smoking duration was 6.6 ± 0.66 years and the average number of cigarettes per smoker per day was 9.8 ± 1.56.

Table 1 shows the measured lipid profile parameters and fibrinogen level in the two groups, levels of cholesterol, LDL-C, and fibrinogen were significantly increased in smokers than non-smokers ($p < 0.0001$). The HDL-C was markedly decreased in the smokers group, while the triglycerides level did not differ.

Table 1: Lipid parameters and fibrinogen level in smokers and non-smokers groups.

Parameters	Smokers (n = 55)	Non-smokers (n = 100)	p-value
Cholesterol (mg/dl)	185.11 ± 4.72	133.31 ± 1.81	< 0.0001
HDL-C (mg/dl)	29.91 ± 0.85	55.14 ± 2.03	< 0.0001
LDL-C (mg/dl)	145.76 ± 3.10	86.28 ± 1.37	< 0.0001
Triglycerides (mg/dl)	126.07 ± 3.81	120.90 ± 5.13	0.4904
Fibrinogen (mg/dl)	423.44 ± 33.91	284.98 ± 4.15	< 0.0001

3.2. The risk of developing cardiovascular disease among smokers based on the reference range of lipid parameters and fibrinogen

The mean levels of lipid profile and fibrinogen in smokers were compared to the reference ranges of the American Heart Association [19] displaying the percentage of smoker who are at risk of cardiovascular diseases. According to the published guidelines, Table 2 shows that 12.73% of the smokers were at high risk of developing CVDs. The HDL-C showed a marked decrease, 92.73% of the whole group with increased risk. The LDL-C level was increased as compared with the reference range, 32.73% of the smokers were highly susceptible to CVDs risk. For the atherogenic index LDL-C/HDL-C, the mean was 5.05 ± 0.17, indicating that the studied smokers were at high risk. Of the 55 smokers, only 16.36% had borderline high triglycerides. The fibrinogen level 423.44 mg/dl was high when compared with the reference range (365 mg/dl) of the American Heart association.

Normal plasma fibrinogen levels range were defined as 200–400 mg/dl, and hyperfibrinogenemia was defined as plasma fibrinogen concentrations greater than 400

Table 2: Mean levels of the lipid parameters and fibrinogen, and risk participants according to the reference ranges.

Lipid Parameters	Mean ± SE (n = 55)	Smokers at the border line of CVDs risk	Smokers at high CVDs risk
Cholesterol (mg/dl)	185.11 ± 4.72	3.64%	12.73%
HDL-C (mg/dl)	29.91 ± 0.85	7.27%	92.73%
LDL-C (mg/dl)	145.76 ± 3.10	45.45%	32.73%
LDL-C/HDL-C	5.05 ± 0.17	18.18%	72.73%
Triglycerides (mg/dl)	126.07 ± 3.81	16.36%	–
Fibrinogen level			
Fibrinogen (mg/dl)	423.44 ± 33.91	27.27%‖	36.36%†

Notes: The American Heart Association guidelines: the total cholesterol optimal range < 200mg/dl, range from 200–239 mg/dl, demonstrates borderline of risk, ≥ 240 mg/dl indicates high risk to CVDs; optimal LDL-C in the range < 100 mg/dl, while 100–129 mg/dl considered as near optimal, 130–150 mg/dl defines the borderline risk and ≥ 160mg/dl the high CVDs risk; HDL-C < 60 mg/dl specifies the group of adult men at the borderline risk, while the high CVDs risk men are classified at < 40 mg/dl; the hypertriglycerideamia denotes borderline risk at 150–190 mg/dl, and ≥ 200 mg/dl represents the high-risk group; the LDL-C/HDL-C ≥ 4.5 indicates high atherogenic risk.

mg/dl [20]. ‖ specifies smokers with fibrinogen level ≤ 400mg/dl, † indicates smokers with fibrinogen level > 400mg/dl.

3.3. Comparing levels of cholesterol, triglycerides, and fibrinogen between atherogenic groups

The study group was stratified according to the LDL-C/HDL-C ratio into low-risk group of less than 4.5 (group I) and high-risk group that had 4.5 and more (group II). The level of cholesterol was higher in group II compared to group I, the difference between the two group was statistically significant (p = 0.018). The mean serum triglycerides was significantly higher in group II than in group1(p = 0.007). Group II, the high atherogenic risk group, showed conspicuous increase in fibrinogen level compared to group I (p = 0.001). All these data are demonstrated in Table 3 and Figure 1.

Table 3: The mean levels of cholesterol, triglycerides, and fibrinogen in smokers atherogenic groups.

Variables	Atherogenic < 4.5 Group I (n = 15)	Atherogenic ≥ 4.5 Group II (n = 40)	p-value
Cholesterol	168.73 ± 7.06	191.25 ± 5.67	0.018
Triglycerides	111.47 ± 5.32	131.55 ± 4.58	0.007
Fibrinogen	293.00 ± 27.21	472.35 ± 43.18	0.001

Note: LDL-C and HDL-C levels were not represented in the variables because they were expressed as LDL-C/HDL-C ratio (atherogenic index).

3.4. Risk estimate for cardiovascualar diseases using LDL-C/HDL-C ratio and fibrinogen level

The risk estimate of having high fibrinogen as a risk factor for cardiovascular events was assessed in smokers using logistic regression analysis (Table 4). No significant association was observed between the level of total cholesterol, LDL-C, or triglycerides. Considerably, the smokers with atherogenic index ≥ 4.5 are 3.96% more likely to have high fibrinogen ≥ 300 mg/dl and hence more vulnerable to cardiovascular diseases (p = 0.026).

Table 4: Frequency of smokers and risk estimate of having high fibrinogen according to the normal and high ranges of total cholesterol, LDL-C, triglycerides levels, and LDL-C/HDL-C ratio.

LDL-C/HDL-C ratio	Fibrinogen level		p-value (OR, 95%CI)
	≥ 300 mg/dl	< 300 mg/dl	
Cholesterol ≥ 200	26	14	0.73 (0.81, 0.24–2.74)
Cholesterol < 200	9	6	
LDL-C ≥ 130	31	15	0.20 (2.58, 0.61–11.04)
LDL-C < 130	4	5	
TG ≥ 150	7	2	0.34 (2.25, 0.42–12.06)
TG < 150	28	18	
Atherogenic ≥ 4.5	29	11	0.026 (3.96, 1.14–13.73)
Atherogenic < 4.5	6	9	

Note: HDL-C was removed from the logistic regression model because all smokers were having HDL-C < 60mg/dl.

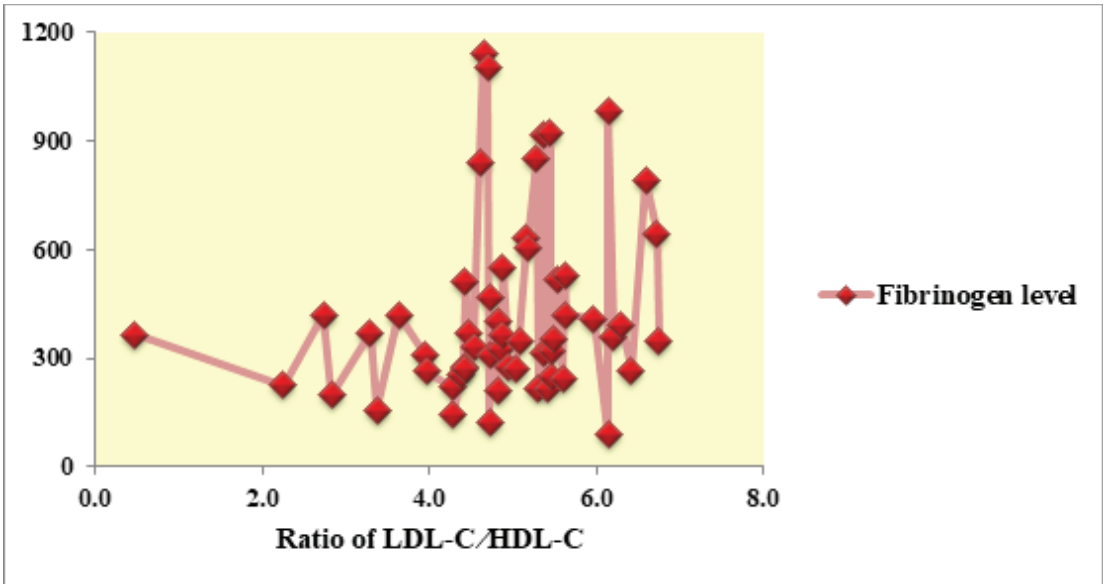

Figure 1: The correlate of fibrinogen level to the LDL-C/HDL-C ratio.

4. Discussion

Smoking has been recognized as an important risk factor for the CVDs, attributed to the alterations of the plasma fibrinogen and lipoprotein pattern [21, 22]. Our study was conducted to evaluate the level of fibrinogen and lipid profile in Sudanese smokers. According to the reference range of the fibrinogen level, the study showed increased mean level of fibrinogen among Sudanese smokers. This result was supported by several global studies, which confirmed an increased level of fibrinogen among smokers [22–24]. In Sudan, a comparative study was done that revealed the increase of fibrinogen level among healthy smokers, whereas the level was decreased among non-smokers and ceased smokers, plasma fibrinogen may remain elevated for several years after cessation [25, 26]. In that scenario, it was proved that a primary role for increased synthesis in producing the hyperfibrinogenaemia associated with smoking: an influential study for smokers showed that cessation from smoking for a period of only two weeks induces a significant decrease in the rate of fibrinogen synthesis by the liver, with a concomitant reduction in the plasma fibrinogen concentration [27].

The association between fibrinogen and carotid atherosclerosis was investigated; high incidence of carotid atherosclerosis was reported among smokers, whilst this trend was not manifested for non-smokers or former smokers [17]. In this study, 92.73% of the smokers showed low HDL-C level $<$ 40mg/dl, and 72.73% of the smokers have $\geq$ 4.5 LDL-C /HDL-C ratio. Highest fibrinogen levels were observed in smokers with high atherogenic risk. Clinical studies have documented that fibrinogen is not only a blood coagulation factor but also an inflammatory marker, influencing leukocyte recruitment, and particularly modulating the adhesive behaviour of the neutrophils [28]. A number of studies reported that a high plasma fibrinogen level is an independent and major risk marker of cardiovascular diseases [29–31]. In a population sample of adults without clinically obvious atherosclerotic disease, elevated fibrinogen levels ascertained to be associated to carotid intima-media thickness, representing a systemic marker of carotid atherosclerosis [32]. In the same consensus, cigarette smoking linked with elevated serum levels of cholesterol, LDL-C, triglycerides, and lower plasma concentrations of HDL-C than non-smoker [33, 34].

Our study does not indicate extreme deviation from normal reference ranges. Similar results were obtained from controlled clinical trial in Polish smokers; higher lipid values with elevated lipid peroxidation products were found when compared with the non-smokers' group, annotating the cigarette-smoking risk in the onset of atherosclerosis and coronary heart disease [35]. Nicotine and carbon monoxide seem to play a major

role in the effect of smoking on vessels. In addition to its acute haemodynamic effects, tobacco not only has an atherogenic effect (endothelial toxicity and changes in lipid profile), but it also facilitates thrombosis (by alteration of platelet functions and elevation of fibrinogen level, haematocrit level and blood viscosity) and vascular contraction (through modification of prostaglandin metabolism and action on catecholamines or decrease of nitric oxide production) [36].

Smoking in adolescence and young adulthood might increase the risk of cardiovascular events [34]. In this study, it is worth pointing out that 60% of the study smokers with age less than 35 years, younger smokers give prediction to longer smoking duration and hence aggravating the risk of dyslipidaemia. Confirmation to this suggestion, the smokers with high atherogenic index are more likely to have higher fibrinogen level increasing their vulnerability to develop cardiovascular events. Our data showed that this linear correlation between fibrinogen and atherogenic index was substantiated by the following equation: Fibrinogen level = 19.49 + 79.08 (the ratio of LDL-C/HDL-C), r = 0.37, p = 0.008. Hence, smokers with LDL-C /HDL-C ratio = 4.5 might have fibrinogen level 375.35 mg/dl.

5. Conclusion

Significant elevation of fibrinogen, LDL-C Levels, and LDL-C /HDL-C ratio concomitant with significant decrease in serum HDL-C concentration were remarked among Sudanese smokers. Smokers with high atherogenic index are more liklely to have increased level of fibrinogen. It was suggested that the increase of fibrinogen level in addition to alterations of lipid profile increase the risk of cardiovascular disease among Sudanese smokers.

6. Limitations of the Study

Overall, the study included a small number of smokers, and little attention was paid to post-study follow-up.

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Conflict of Interest

The authors declare no conflict of interest.

Authors' Contribution

Hani Yousif Zaki and Reem Sideeg Mustafa participated in designing the study, collection of data, and the practical work. Hani Yousif Zaki and Hiba Mahgoub Ali interpreted the data. Badreldin Elsoni Abdalla made amendments on the manuscript draft. All authors meticulously revised and approved the final manuscript.

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