Body mass index, fibrinogen and factor VII activity in male smokers and non-smokers living in an Urban industrialized

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ABSTRACT

Differences in haemostatic parameters have been reported among smokers and non-smokers. However the relationships of these parameters with other risk factors of cardiovascular diseases have not been fully determined in Nigerians. We therefore aimed at assessing the relationship between fibrinogen, factor VII (FVII), age, body mass indeks (BMI), systolic blood pressure (SBP) and diastolic blood pressure (DBP) in smokers and non-smokers living in an Urban Nigerian city. We studied 104 male Nigerians grouped into non-smokers (n= 74) and smokers (n= 30). Fibrinogen was measured using the clot weight method of Ingram and FVII was assayed by the bioassay method. Mean fibrinogen and FVII were found to be higher in smokers than non-smokers. There was no relationship between FVII and age (r= -0.0458) in non-smokers and a weak association was found between FVII and age in smokers (r= 0.3191). Both SBP and DBP were significantly associated with BMI in smokers (r= 0.6332, p= 0.0002) for DBP and (r= 0.4869, p= 0.0064) for SBP. Fibrinogen was only associated with DBP in non-smokers (r= 0.3273, p= 0.0047). FVII and fibrinogen were found to be higher in smokers compared to non- smokers, the difference was not statistically significant (p= 0.1965). The strength of the association of BMI and fibrinogen with blood pressure is higher for DBP in Nigerians. Extensive population studies should be conducted on smokers and non-smokers to confirm these associations.

Key Words: Smoking, Factor VII, Fibrinogen.

INTRODUCTION

Factor VII (FVII) is a vitamin K dependent plasma serine protease which is very important in the initiation of the extrinsic pathway of blood coagulation. It is been increasingly associated with the development of cardiovascular diseases (CVD) in the Europeans and Caucasian populations[1]. The role of high levels of FVII and fibrinogen in the development of CVD as well as the plasma levels of these coagulation factors have not been fully determined in Africans.

Plasma levels of FVII vary over a wide range in the general population and several fac-

tors ranging from age, sex, body mass index (BMI), the use of oral contraceptives, and dietary fat have been associated with FVII levels[1-3]. The levels of FVII in the plasma increases with age in both sexes, with a greater increase in women after the age of 45 years; a situation which suggests dependence on the hormonal status of the women, this appears to be supported by a decrease in FVII levels in postmenopausal women taking percutaneous oestrogen when compared to those not receiving it[4].

Several studies have given conflicting results on the association between FVII clotting activity and the risk of ishaemic CVD[5-7]. While high levels of FVII were independently associated with an increase in the risk of coronary events in middle aged men in the Northwick Park Heart study (NPHS), a subsequent study, by the same group showed that FVII levels was predictive for fatal, but not for, non-fatal myocardial infarction[5,6]. Similarly high levels of FVII have not been found to be predictive of thrombotic events in patients with vascular disease, coronary artery disease, and venous thrombosis by other studies[8,9].

A number of reasons have been postulated to have contributed to the discrepancy in results obtained by different investigators; these include the different methods used in evaluating FVII, the use of thromboplastin of different origins, and the fasting status of the subjects[10-13]. A strong positive relationship between plasma fibrinogen and CVD has been widely reported by several prospective studies[14-16].

In spite of the evidences associating fibrinogen with the risk of coronary heart diseases (CHD), in clinical practice, fibrinogen is not commonly used to assess the CHD risk, as in the case of FVII. A number of reasons have been suggested to be responsible for this and they include: lack of consensus on measurement methods, lack of widely accepted standards for abnormal values, high costs of the biochemical assays and lack of information on the effect on CHD risk of lowering plasma fibrinogen[17].

While ethnic and racial differences in the mean fibrinogen concentration and FVII activity have been widely reported in the Europeans and Caucasians with some evidences for genetic basis for this variation, limited studies have been conducted on Africans[18,19]. We therefore assessed the level of FVII, fibrinogen and their relationship to BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP) and smoking status in men working in a major industrial city in Nigeria a populous African nation.

MATERIALS and METHODS

Subjects

One hundred and four males living in Warri a major industrial city in Nigeria were studied. They were grouped into smokers (n= 30) and non-smokers (n= 74). Smokers were defined as people who regularly smoked at least one cigarette per day for at least five years. All the subjects had no clinical evidence of disease(s). Full and informed consent were obtained before commencement. Data on age, smoking habits and medical history were obtained by verbal interview. Weight was measured on a balanced scale on participants with their shoes off. Heavy outer garments were removed to minimize error. Seated brachial blood pressure was measured after a five minutes rest. The BMI was calculated using the formula; BMI (kg/m^2)= weight (kg)/height $(m)^2$.

Blood Samples

5 mL of blood was collected from the cubital vein using a plastic syringe while applying tourniquet lightly over the arm until blood flow was established. Stasis was avoided during blood collection to prevent activation of clotting factors. 4.5 mL of blood was transferred into a plastic tube containing 0.5 mL of 3.8% sodium citrate. Blood and anticoagulant were mixed gently but thoroughly.

Plasma was separated by centrifugation at 2500 g for 15 minutes to obtain platelet poor plasma. Plasma samples were preserved on ice and analyzed for FVII and fibrinogen within two hours of collection. The plasma fibrinogen was estimated using the clot weight method of Ingram[20]. FVII assay was done by the bioassay method[21].

Statistical Methods

All data were analyzed using Graph pad INSTAT™ statistical package. Means of fibrinogen, FVII and other variables were compared using the Mann-Whitney U test. Simple Pearson's correlations were computed to describe the univariate association between FVII, fibrinogen and other independent variables (BMI, age, SBP and DBP). A p value of < 0.05 was considered significant.

RESULTS

A total of 104 male Nigerians aged 30-60 years comprising of 30 smokers and 74 non-smokers were studied.

The means of variables studied in smokers and non-smokers were compared in Table 1. Mean FVII activity was higher in smokers than non-smokers with a mean difference of 1.5%, mean fibrinogen was also higher in smokers than non-smokers (mean difference 0.28 g/L) with a borderline significance (p= 0.0592). Mean BMI differs in smokers from non-smokers by 0.16 kg/m^2. Both SBP and DBP were higher in non-smokers than smokers. FVII correlated poorly with BMI, SBP and DBP in both smokers and non-smokers. There was a weak correlation with age in non-smokers (r= 0.325, p= 0.0857) (Table 2), a significant and positive association was found between fibrinogen and DBP in non-smokers (r= 0.3273, p= 0.0047) but not in smokers Table 3. The SBP was also weakly correlated with fibrinogen in smokers (r= 0.325, p= 0.0607). Table 4 shows the correlation coefficient between BMI and blood pressure in both smokers and non-smokers. The BMI was significantly associated with blood pressure (SBP and DBP) in smokers, r= 0.4869 and p= 0.0064 for SBP and r= 0.6332, p= 0.0002 for DBP. No association was found between BMI and blood pressure in non-smokers. The means of the variables studied according to age groups for non-smokers is shown in Table 5. A gradual decline in means of FVII and fibrinogen was observed while BMI slightly increased across groups; however there is no significant difference in the means of these parameters across the various age groups.

DISCUSSION

Several epidemiological surveys had reported an association between FVII, fibrinogen and other markers of CVD[14-16,22]. We studied FVII and fibrinogen and their relationships to some risk factors of CVD in smokers and non-smokers. We found a higher FVII activity in smokers than non-smokers

Table 1. Mean of haemostatic variables and other risk factors in smokers and non-smokers

	Smokers (n= 30)	Non-smokers (n= 74)	
Variable	n (SD)	n (SD)	p value
FVII (%)	99.3 (5.09)	97.8 (5.7)	0.1965
Fibrinogen (g/L)	3.25 (0.70)	2.97 (0.66)	0.0598
BMI (kg/m^2)	26.2 (5.0)	26.0 (4.0)	0.8716
SBP (mmHg)	118.7 (18.7)	123.8 (20.0)	0.2194
DBP (mmHg)	82.5 (20.0)	85.5 (12.5)	0.2923
Age (years)	44.8 (6.2)	43.2 (6.8)	

Table 2. Correlation coefficients between FVII and other risk factors

Risk factors	Smokers (n= 30)	Non-smokers (n= 74)
FVII		
Fibrinogen	0.0951	0.0673
BMI	0.1957	0.0785
SBP	0.1591	0.0796
DBP	0.1100	0.1474
Age	0.3191	-0.0458

Table 3. Correlation coefficients between fibrinogen and other risk factors

Risk factors	Smokers (n= 30)	Non-smokers (n= 74)
FIBRINOGEN		
FVII	-0.0951	0.0673
BMI	-0.1214	0.0673
SBP	0.3251	0.2206
DBP	0.2215	0.3273*
Age	0.1367	-0.0892

* p= 0.0047.

Table 4. Correlation coefficient between BMI and blood pressure

Risk factors	Smokers (n= 30)	Non-smokers (n= 74)
BMI		
SBP	0.4869*	0.0725
DBP	0.1141	0.6332**

* p< 0.01, ** p< 0.001.

(mean difference 1.5%) the difference however was not statistically significant. Fibrinogen was also found to be higher in smokers than non-smokers as has been previously reported[22,23].

A weak association between fibrinogen and age was also found, this agreed with the findings of Andrzej O et al and differed from other studies where a strong relationship between fibrinogen and age had been reported in smokers[22-25]. The difference in the results obtained from our study could be explained by the relatively small population of smokers and non-smokers in this work as well as the number of cigarette smoked.

Also as in a previous study, fibrinogen was not found to be related to BMI in both smokers and non-smokers alike[24]. Our study also confirmed an association between fibrinogen and blood pressure in non-smokers as has been previously reported, this however is not unexpected as the association of fibrinogen with the presence and extent of atherosclerosis, stenosis of the coronary vessels and peripheral arterial diseases has been widely reported[26-29]. Conversely in smokers, there was no relationship between fibrinogen and blood pressure. We could not explain the lack of association between fibrinogen and blood pressure in smokers obtained in our study, especially when plasma fibrinogen concentration was found to be higher in smokers than non-smokers. The higher mean SBP and DBP obtained for non-smokers in this study could suggest a lack of association between smoking and blood pressure, however the small population of

Table 5. Means of fibrinogen, FVII, and BMI according to age groups in smokers

	Age groups in years			
Parameter	**30-49**	**40-49**	**50-59**	**p value**
FVII	98.3 (5.8)	97.3 (6.2)	97.9 (6.0)	NS
BMI	25.0 (3.8)	26.4 (3.7)	26.6 (5.1)	NS
Fibrinogen	3.0 (0.8)	3.0 (0.6)	2.8 (0.6)	NS

NS: Not significant.

smokers and non-smokers may not support this reasoning.

As has been previously reported, we did not find any association between FVII and age and no significant associations between FVII, BMI, and blood pressure in both smokers and non-smokers as found by other workers[22,23,26]. A positive association between BMI and blood pressure was seen in smokers. Even though both DBP and SBP were positively correlated with BMI, the strength of the association was higher with DBP (r= 0.6332, p= 0.0002) than SBP (r= 0.4869, p= 0.0064). No relationship was observed between BMI and blood pressure for non-smokers. Again the discrepancy in the relationship between BMI and blood pressure in smokers and non-smokers could not be readily explained. It is possible that other confounding variables like alcohol intake and family history of hypertension which we did not obtain may have more impart on non-smokers than smokers. However, it could be inferred from these findings that, a combination of smoking and high BMI is more likely to raise the DBP.

Despite the small sample size of this study, we believe that the study has provided baseline information on the relationship between fibrinogen, FVII and smoking habits in Nigerians.

In conclusion, we studied the association between FVII, fibrinogen, BMI and blood pressure in both smokers and non-smokers. We found a strong association between BMI and blood pressure in smokers, higher mean FVII activity in smokers and a weak association between fibrinogen, age and BMI. High levels of FVII, hyperfibrinogenemia may lead to CHD in African smokers. An extensive population study on haemostatic parameters and other risk factors for CVD needs to be done on Nigerians to confirm our observations.

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