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Enhanced fibrinolysis in Nigerians—probable contributory factor to low prevalence of Atherosclerosis in the Nigerian

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Summary

Results of more detailed study of the fibrinolytic enzyme system in Nigerians is reported. A relatively short euglobulin lysis time (ELT, range 75·87–196·08 units) in the males was observed, while a longer time (49·50–98·04 units) was observed in females aged 19–35 years. The mean concentrations of fibrinogen (0·41 ± 14 g/100 ml) and plasminogen (2·45 ± 1·03 Casein units) which are reported, the latter for the first time in this population are similar to values in other populations. Although plasminogen/plasmin inhibitors were not separately determined in this study, results of the ELT suggest that this was probably due to increased activator activity, and supports a previous suggestion that this increased activator activity may be a mechanism of the enhanced ELT in the males examined.

Résumé

On signale les résultats d'une étude plus pousseé du système d'enzyme fibrinolytique chez les Nigerians. Il a été remarqué que le temps de lyse de l'euglobulins (ELT) est court chez les hommes, et plus long chez les femmes âgées de 19 à 35 ans. Les concentrations de fibrinogène et de plasminogène que l'on signale sont semblables a celles remarqués chez d'autres populations (et, en ce qui concerne le plasminogène, c'est la première fois que l'on constate cette ressemblance). Bien que les inhibiteurs du plasminogene et de la plasmine waient pas été séparément déterminés au cours de cette étude, less résultats de l'ELT laissent supposer que ceci est probablement dû à une activité accrue des activeurs, et viennent à l'appui d'une proposition préalable selon laquelle ceci serait un méchanisme d'une fibrinolyse rehaussée chez les hommes dans les populations africanles.

Introduction

Atherosclerosis and myocardial infarction are reportedly rare among Black Africans (Dada *et al.*, 1969; Osuntokun *et al.*, 1969 and Williams *et al.*, 1975). Information on the probable cause(s) of this relatively healthy state such as blood lipid and cholesterol levels, and haemostatic parameters is scanty (Howell, 1965; Menon, 1968; Walker, 1961 and Lackner & Johnson, 1967). Although it has been suggested that platelets contribute to a large measure in the actiogenesis of the disease in Caucasian population groups, reduced fibrinolysis at sites of atheromatous plaques have also been observed in these populations (Peabody *et al.*, 1974). In the rapidly changing Nigerian society, it was considered essential that the factors that are known to be involved in these diseases in other populations should be examined as fully as possible. This communication describes in greater detail than previously (Howell, 1965), results of studies of some aspects of the fibrinolytic enzyme system in Nigerians. This was considered an essential prelude to a more detailed examination of the factor(s) responsible for the less severe manifestations of atherosclerosis in our own and other Black African populations (Williams *et al.*, 1975).

Materials and methods

Blood samples

These were collected between 0930 and 1030 on each day of the test by clean vene-puncture from eighty-six blood donors and other volunteers aged between 17 and 47 years. There were eighty males and six females. The females were in the 19–35 age range and were not on any drugs at the time of the test. Each sample was mixed with 3·8% sodium citrate (nine parts of blood to one part of citrate) and plasma was

obtained after centrifugation at 22°C at 3000 *g* for 10 min.

The following tests were performed on each sample: (1) modified one-stage prothrombin time (Hardisty & Ingram, 1965); (2) fibrinogen concentration by the clot-weight method (Hardisty & Ingram, 1965), and by Alkjaersig's modification of the method of Ratnoff & Menzie (1951); (2) euglobulin lysis time (ELT) by standard technique (Cash, 1966); (4) plasminogen assay by the modified Caseinolytic method (Alkjaersig, Fletcher & Sherry, 1959).

Results

The mean prothrombin time was 14·11 ± 1·63 s (1 s.d.). Details of this study which formed part of a programme aimed at the setting up of a Thromboplastin standard is reported in full elsewhere (Essien, 1974).

Fibrinogen concentration determined by the Biuret and Clot-weight methods (Fig. 1) gave respective mean concentrations of 0·41 ± 0·14 and 0·34 ± 12 g/100 ml. The correlation coefficient of the results obtained by both methods (r) was 0·83.

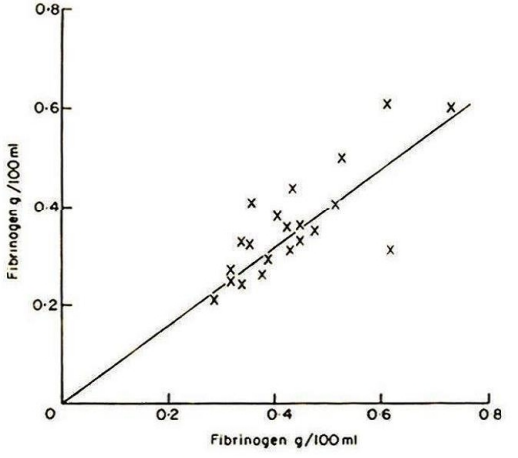

FIG. 1. Relationship of fibrinogen concentration by Biuret and Clot weight methods. Ordinate: Concentration by Clot weight method. Abscissa: Concentration by Biuret method. Normal 0·44 g/100 ml (range 0·21–0·53 g/100 ml).

The results of the ELT was in the range of 51–131·8 min (75·87–196·08 units). There was no relationship to age or ABO blood groups (Table 1). The mean ELT in females, 152·00 ± 24·65 minutes (56·61–78·52 units) was significantly longer than the value in males ($P < 0·005$).

TABLE 1. Relation of ELT to ABO blood groups in male subjects

ABO Blood Groups	ELT (Units)
A+	75·47–252·14
B+	82·77–170·62
O+	76·86–198·93
AB+	68·19–165·15

The ELT value for each ABO blood group was compared with the value of the whole group of male subjects examined (see Table 3). A unit is the reciprocal of the Euglobulin Lysis time in minutes.

TABLE 2. Frequency distribution of plasminogen concentration in sixty-three healthy adult Nigerians

Concentration (Casein units/ml)	Frequency of observations
0·0	0
0·5	2
1·0	9
1·5	11
2·0	11
2·5	12
3·0	9
3·5	5
4·0	3
4·5	1

Plasminogen concentration of sixty-three volunteers reported for the first time in this population was in the range of 0·5–4·5 casein units (mean 2·45 ± 1·03 casein units). The distribution as shown in Table 2 was normal. These results are summarized in Table 3.

Discussion

The results of this study confirm a previous single report (Howell, 1965) of enhanced fibrinolysis in Nigerians. It extends this previous finding with estimation of plasminogen and fibrinogen concentrations. These observations are in essential agreement with an earlier preliminary report (Essien, 1974) and in some respect, with results of similar studies from East African countries and from South Africa (Lackner & Johnson, 1967 and Shaper *et al.*, 1965).

TABLE 3. Summary of results of fibrinolytic parameters

Activity measured	Concentration
(1) Prothrombin time (112)‡	14·11 ± 1·63 s
	1·00 ± 0·11 (ratio*)
(2) Fibrinogen concentration (23)	130–690 mg/100 ml (clot weight)
	220–460 mg/100 ml (Biuret method)
(3) Euglobulin lysis time	75·87–196·08 (males)
(M = 80)	49·50–98·04 (females)
(F = 6)	
(4) Plasminogen concentration (63)	0·50–4·51 casein units/ml.

* The ratio of the mean clotting time of each sample was determined against the grand mean clotting time of all the samples. The figures in parenthesis refer to the number of subjects examined. ‡ The additional number tested formed part of the thromboplastin standardization programme.

The mean fibrinogen concentration obtained in this series determined chemically was 0·41 ± 0·14 g/100 ml. The mean concentration as determined by the clot-weight method was 0·34 ± 0·12 g/100 ml. There was good correlation between both values (r = 0·83, Fig. 1). Thus with availability of a good chemical balance, quantitative fibrinogen estimation by direct weight gives a reliable, though somewhat lower, result. It is however unsuitable for use in acquired hypofibrinogenic states partly because of the difficulties of obtaining accurate weights at low concentrations, and partly because in acute DIC states, the clots observed were friable and fragmented. These results of fibrinogen concentration lie within essentially the same range as those values obtained in Caucasian populations (Hardisty & Ingram, 1965). It thus differs from an earlier report of higher fibrinogen concentration in Black Africans (by 50–100%) than in South African Caucasians (Deegan, Gilles & McGregor, 1956), and is in agreement with results in Uganda (Alpidovsky *et al.*, 1974).

Euglobulin lysis time as determined in this report is known to be affected mainly by concentrations of fibrinogen, plasminogen and resting level of activator since inhibitors are largely excluded.

Our mean normal value of 91·4 ± 40·4 min (range 51–131·8 min 75·87–196·08 units) in males is shorter than values (100–300 min, 33·3–100·0 units) (Nilsson, 1971) in Caucasian populations. In this respect, our findings are in agreement with studies in other African populations (Menon, 1968; Lackner & Johnson, 1967 and Shaper *et al.*, 1965). Females exhibited longer ELT than males. The reason for this enhanced activity in our male population was not examined. It has, however, been suggested that this might be due to high plasminogen activator activity in the Africans (Lackner & Johnson, 1967).

Plasminogen concentration determined by the Caseinolytic method was in the range of 0·5–4·51 Casein units (mean 2·45 ± 1·0). This result can reasonably be compared with those in other populations where a similar method of estimation was employed and where, for instance, the normal plasma concentration was 4·4 ± 0·5 Casein units (Ogston, Benneth & Ogston, 1971). Although the use of streptokinase to estimate the concentration of human plasminogen is liable to some errors because of the complex nature of the reactions involved (Nilsson, 1971; and McClintock *et al.*, 1974), it has been widely used and valid conclusions have been, and can still be drawn from results obtained from such studies.

From these results, it is clear that evidence of enhanced fibrinolysis observed in the male population was primarily detected in the short ELT and not in changes in either fibrinogen or plasminogen concentrations. It is suggested that evidence of enhanced fibrinolysis observed in this and other studies, may be a factor in the low prevalence of atherosclerosis observed in this population.

The reason(s) for the marked difference between the male and female values is being examined.

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