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LUPUS ANTICOAGULATION IN AFRICAN WOMEN WITH RECURRENT ABORTIONS

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ABSTRACT

Objective The presence of the lupus anticoagulant (LA), an auto antibody has been implicated as a marker for first trimester spontaneous abortions as well as second and third trimester foetal deaths in the Caucasians. There is paucity of information on LA in African women where recurrent abortion and obstetrics complication are still common. Our aim therefore is to determine the prevalence of lupus anticoagulant in Nigerian women with recurrent abortion.

Subjects and Methods A total of seventy-three pregnant women were studied. Twenty-three of them had history of recurrent abortions; they were compared with 50 without obstetric complications as controls. Coagulation studies using the kaolin clotting time were carried out on their plasma samples. Mixing experiments were conducted on samples with prolonged clotting time in order to detect the presence of the lupus anticoagulant. The anticoagulant was considered present if the kaolin clotting time ratio is greater than or equal to 1.2.

Results Nineteen {82.62%} of the patients with recurrent abortion had normal kaolin clotting time, one {4.35%} had subnormal clotting time, while 3{13.04%} had a prolonged kaolin clotting time. The kaolin clotting time ratio was greater than 1.2 In one (4.35%) of the patients with recurrent abortions signifying the presence of the lupus anticoagulant. Four (8%) of the pregnant controls had subnormal kaolin clotting time, 44(88%) had normal clotting time while 2(4%) had prolonged clotting time. The lupus anticoagulant was present in one (2%) of the pregnant controls.

Conclusion A 4.35% prevalence of LA among Nigerians with Recurrent foetal loss may necessitate the screening of pregnant women with history of recurrent abortion for the lupus anticoagulant. We recommend that screening for lupus anticoagulant should be part of the routine investigation for women with recurrent spontaneous abortions.

KEY WORDS: ***Recurrent Abortions, Pregnant Women, Lupus Anticoagulant, Kaolin Clotting time***

INTRODUCTION

The occurrence of spontaneous acquired inhibitor of blood coagulation had been widely reported[1-3]. The lupus anticoagulant (LA) an acquired coagulation inhibitor belongs to a spectrum of antiphospholipid antibodies including the biological false positive tests for syphilis and the anticardiolipin antibodies. Both the lupus anticoagulant and anticardiolipin antibodies have been shown to be associated with arterial and venous thrombosis, thrombocytopeania, recurrent foetal loss, and neurological diseases which are collectively known as the antiphospholipid antibodies syndromes [4-6].

The lupus anticoagulant, an immunoglobulin (IgG, IgM or both), was first described in 1952 by Conley and Hartman in two patients with systemic lupus erythematosus and it was erroneously named "lupus anticoagulant[7]. However it has since been discovered in numerous other clinical conditions including apparently healthy individuals [8]. The presence of LA is usually suspected on finding a prolonged phospholipid dependent clotting test [4] which in most cases are not associated with a bleeding tendency but paradoxically thrombosis hence the name lupus anticoagulant is a misnomer [2,7,9].

Foetal loss, often recurrent, is one of the most important clinical manifestations of LA [10,11]. In women with or without systemic lupus erythematosus the presence of LA has been reported to be associated with a high incidence of first trimester spontaneous abortions and second or third – trimester foetal deaths[12-14]. The mechanism for the foetal loss in patients with LA is still subject of research, but inhibition of prostacyclin production or release had since been postulated as a likely pathogenetic mechanism[15]. In Caucasian women, the presence of this autoantibody has been implicated as a marker for recurrent first – trimester spontaneous abortions, as well as for second and 3rd – trimester foetal deaths[16]. Treatment with prednisolone and aspirin has been advocated as a method of improving pregnancy outcome in these patients[13]. However, to our knowledge, these laudable therapeutic measures are still not

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routine in most hospitals in the developing countries where recurrent abortion and intrauterine foetal deaths are not uncommon due to paucity of information on LA and its obstetrics manifestations. Our aim therefore was to determine the prevalence of LA in women with recurrent abortions in our community, with view of proffering therapeutic interventions.

SUBJECTS AND METHODS

Subjects

The study involved 23 pregnant women mean age 26 years, mean gestational age 29.1 weeks with history of 2 or more spontaneous abortions or history of 2 or more intrauterine foetal deaths in their previous pregnancies.

50 pregnant women apparently healthy without history of the above conditions served as controls. All patients were recruited from the antenatal clinics of the University of Benin Teaching Hospital and Central Hospital Benin City. Their informed consents and approval of the hospital ethic committee were obtained before commencing the study.

Methods

Blood samples were obtained by clean venu puncture into a clean plastic tube containing 0.129 trisodium citrate in a ratio of one part of anticoagulant to nine parts Blood. Platelet poor plasma was prepared by centrifuging at 2,500 g for 15 minutes.

The kaolin clotting time (KCT), tests were carried out, by incubating 0.2 ml kaolin suspension (20 g / L in tris Buffer PH 7.4) for 3 minutes at 370 c. The time from the addition of 0.2 ml of 0.025 calcium chloride to the formation of a clot was recorded, the procedure was carried out in duplicates for each samples and the average time was taken as clotting time[12,17].

Mixing experiments were performed on test and control plasma samples with prolonged clotting time in the following proportions of normal pooled plasma (NP) to test plasma (NP / TP) 100 / 0,80 / 20,50 / 50,80/20 and 100/ 0 as previously described [12,17]

Detection of the lupus anticoagulant[17]: The KCT ratio which is the ratio of KCT at 20% test plasma to KCT at 100% normal control plasma of greater than or equal to 1.2 was taken to signify the presence of the Lupus anticoagulant i.e.

$$\frac{\text{KCT (80\% N: 20\% Test)}}{\text{KCT 100\%}} \supseteq 1.2$$

Statistical Analysis:

Test of significance between the prevalence of LA in pregnant control and recurrent foetal loss was done using Fischer's exact test. $P < 0.05$ was taken to be statistically significant.

RESULTS

Table 1 shows the KCT ranges of the 23 patients with recurrent abortions and that of the pregnant controls, 19 (82.62%) of the patients with recurrent abortions had a normal KCT, 1 (4.35%) had subnormal KCT, while 3 (13.04%) had prolonged KCT. Four (8%) of the pregnant controls had subnormal KCT, 44 (88%) had normal KCT while 2 (4%) had prolonged KCT. The prolonged clotting times of two of the patients with recurrent abortions were corrected by varying mixtures with normal pooled plasma (Figure 1). One (4.35%) was not corrected by mixing with

Table 1: **KCT Ranges of Patients and Controls**

Patient's Group	No of Patients		
	KCT<60 seconds	KCT 60-110 seconds	KCT>110 seconds
Recurrent Foetal loss (n=23)	1(4.35)	19(82.61)	3(13.04)
Pregnant Control (n=50)	4(8)	44(80)	2(4)

Figure1: **KCT Ranges of Patients and Controls**

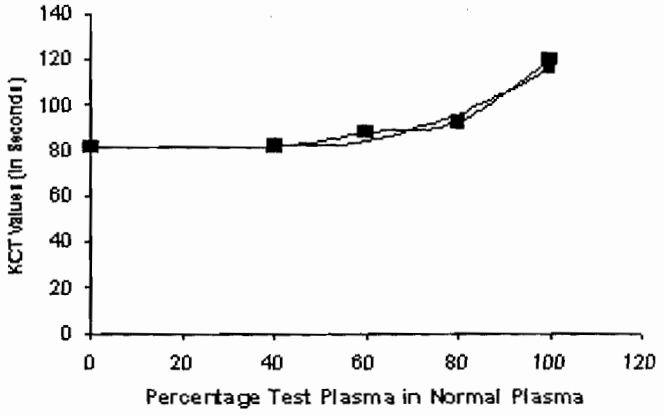


Table 2: **Prevalence of LA in Recurrent Foetal Loss and Controls**

Patient's Group	Lupus Anticoagulant Present	Absent
Recurrent foetal loss (n=23)	1(4.35)	22(95.65)
Pregnant Control (n=50)	1(2)	49(98.00)

P = 0.5339

Percentages in parentheses

Figure 2: **KCT Values of Test Plasma (Recurrent abortion) in various proportions of Normal Plasma (KCT>1.2)**

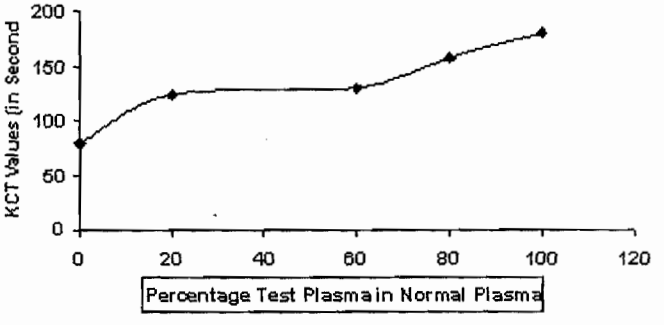


Figure 3: **KCT Values of Test Plasma in various proportion of Normal Plasma in Pregnant control (KCT Ratio>1.2)**

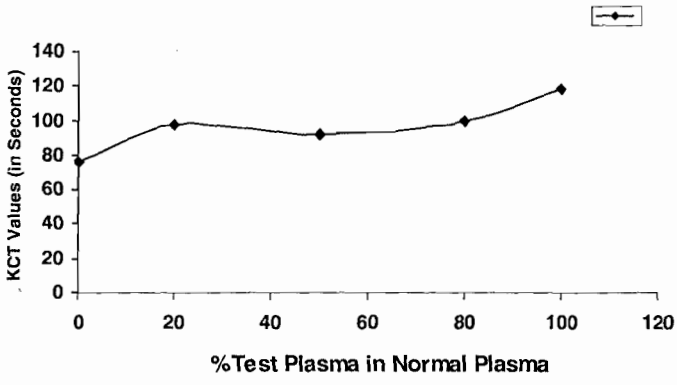
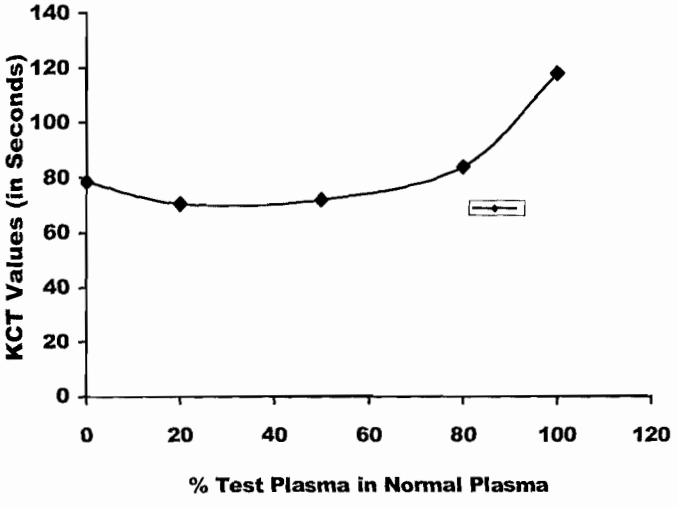


Figure 4: **KCT Values of Test Plasma in Various proportions of Normal Plasma in Pregnant control (KCT Ratio<1.2)**



normal plasma and the KCT ratio was greater than 1.2 suggesting the presence of LA (Figure2).

The prolonged clotting time of one of the pregnant controls was corrected by normal plasma (Figure 3), while one (2%), was not corrected (Figure 4). Figures 1 and 3 shows type 4 pattern of mixing curves signifying the absence of the lupus anticoagulant while figure 2 and figure 4 show type 2 patterns indicating the presence of LA and a coagulation factor deficiency. Both samples also have KCT ratio of over 1.2 further confirming the presence of the lupus anticoagulant.

Table 2 shows the prevalence of LA in patients with recurrent foetal loss and controls. Of the 23 patients with recurrent foetal loss, one, representing 4.35% had LA while one (2%) of the pregnant controls had LA. There is no statistically significant difference between the prevalence of LA in recurrent foetal loss and pregnant control (p = 0.5339).

DISCUSSION

Intrauterine deaths have been widely reported in pregnant women with circulating anticoagulant[15,18-20]. The wide arrays of diagnostic methodologies[21] involved in the detection of the lupus anticoagulant (LA) coupled with the fact that a highly discriminant test is still elusive in developing countries like Nigeria[22] might have contributed significantly to the paucity of information on LA and its obstetric manifestations in sub Sahara Africa. In this study, a 4.35% prevalence of LA was found in pregnant women with history of recurrent abortions and/or foetal deaths. This was not found to be statistically significant when compared with a prevalence of 2% in pregnant controls (p = 0.5339). The prevalence of 4.35% LA in women with recurrent spontaneous abortion obtained in this study defers slightly from the incidence of 5.2-48.2% obtained in previous studies. [2,3,24] This probably means that occurrence of LA in women with multiple spontaneous abortions does not enjoy racial predilection.

The incidence of 2% in normal uncomplicated pregnancies agrees with the work of Hougie and Bird who also reported a less than 5% incidence in the same category of people[25].

The actual prevalence of LA in women with recurrent spontaneous abortions may be higher than the *4.35%* found in this study, as the large percentage of normal pooled plasma to test plasma used in this study, might have eliminated some individuals with weak LA. Further more the KCT tests used in this study might not have been sensitive to all the isotopes of LA[22].

Different types of mixing curves had been described for LA.The type 4 pattern was observed in two patients whose prolonged clotting times were not due to LA, while the type 2 mixing curves were observed in the two patients (one patient with recurrent abortion and one pregnant control) with LA[17].

Although it remains controversial whether LA, is causal or consequence of its clinical manifestations a better pregnancy outcome has been reported when women with recurrent spontaneous abortions are placed on treatment[13].

Even though, the prevalence of LA in pregnant women with recurrent spontaneous abortion found in this study is 4.35%, we believe that the presence of this autoantibody, which has been implicated as an important clinical marker for recurrent first and second trimester spontaneous abortions may contribute to this obstetrics complication in African women. We therefore recommend that all African women with history of spontaneous abortions or intrauterine foetal deaths should be screened for LA early in pregnancy. Those who have the anticoagulant should be placed on appropriate treatment.

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