

Lupus anticoagulant in Nigerian women with preeclampsia

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Summary

Objective

The Lupus Anticoagulant (LA) which used to be known for its interference with coagulation studies in the 1950s,¹ has now been recognised to be associated also with diverse disease conditions in the developed countries. Our aim therefore was to determine the prevalence of the lupus anticoagulant (LA) in women with pre-eclampsia and controls.

Subject and Methods

A total of seventy-six pregnant women, were studied, twenty-six pre-eclampsia and fifty who were apparently healthy served as controls. The Kaolin clotting time test (KCT) was performed in duplicates on plasma samples from subjects and controls. Mixing ratio was calculated in order to determine the presence of the lupus anticoagulant, Kaolin clotting time ratio of greater than or equal to 1.2 was taken to signify the presence of the lupus anticoagulant.

Results

Eleven (42.3%) of the women with pre-eclampsia had prolonged KCT as against 2(4%) of the pregnant control. The clotting time of 7 of the 11 pre-eclampsia with prolonged KCT, were corrected by normal plasma, while 4 were not corrected. The KCT ratio of all 4 were greater than 1.2 signifying the presence of LA (15.4% prevalence). One (2%) of the pregnant control had KCT ratio greater than 1.2 (2%) prevalence of LA.

Conclusion

A number of Nigeria women with pre-eclampsia also have the lupus anti-coagulant therefore African women with pre-eclampsia should be screened for the presence of lupus anti-coagulant.

Keywords: *Lupus anticoagulant, Kaolin clotting time, Pregnancy, Pre-eclampsia.*

Résumé

Objectif

Le Lupus anti-coagulant (LA) qui était autrefois connu pour son interférence avec des études sur la coagulation dans les années cinquantes est aujourd'hui accepté d'être associée également avec les divers états des maladies dans les pays développés. Notre objectif est donc de déterminer la fréquence du lupus anti-coagulant chez des femmes avec la pré-éclampsie et des contrôles.

Sujet et Methodes

Un total de soixante sieze femmes enceintes ont été étudiées, vingt-six avec prééclampsie et cinquante qui étaient apparemment en bonne santé tiennent lieux de contrôles. Le temps d'épreuve du coagulation de kaolin (Kaolin clotting time test KCT) a été opéré en deux exemplaire sur les préélévément du plasma des sujets et des contrôles. Des expériences de mixage ont été effectuées sur des préélévément avec le temps prolongé de la coagulation. La proportion du temps de la coagulation du Kaolin Lupus anti-coagulant, la proportion du temps de la coagulation du kaolin de plus de ou égal à 1, 2, était noté de signifier la présence du lupus anticoagulant.

Resultats

Onze soit 42,3% des femmes atteintes de la pré-éclampsie avaient KCT prolongé par rapport à 2 soit 4% des femmes enceintes, contrôles. Le temps de la coagulation chez 7 entre 11 pré éclampsies

avaient KCT prolongé ont été corrigés grâce au plasma normal tandis que 4n' étaient pas corrigé. La proportion KCT de tous les 4 était plus de 1, 2 ce qui indique la présence de LA une fréquence de 15,4%.

Un soit 2% des femmes enseintes contrôles avaient une proportion KCT de plus de 1, 2 (fréquence de LA étant 2%).

Conclusion

Un certain nombre de femmes nigériane atteintes de la pré-éclampsie souffrent également du Lupus anti-coagulant, donc femmes africaines atteintes de la pré eclampsie devraient subi un test de depistage pour la presence du lupus anti-coagulant.

Introduction

The lupus anticoagulant (LA), a circulating inhibitor of blood coagulation, has generated a lot of interest in the past two decades¹. This acquired inhibitor which interferes with the activation of prothrombin by the prothrombin activator complex (Factor Xa Factor V, Calcium and Prospophilipid)² was first discovered in 1952 in a woman with lupus erythematosus, hence the name lupus anticoagulant.³ However, it has since been discovered in other clinical settings including women with recurrent spontaneous abortions, pre-eclampsia,^{4,5} human immuno deficiency syndrome, psychiatric illness and other neurological disorders.^{4,5} LA has not been associated with abnormal bleeding in most patients except in the presence of thrombocytopenia, hypoprothrombinemia or a qualitative platelet defect,⁶ but has paradoxically been linked with thrombosis in some cases.^{3,4,5}

Although various screening tests like the activated partial thromboplastin time (APTT), Tissue Thromboplastin inhibition test (TTI), the Kaolin Clotting Time of platelet poor plasma have been used for the detection of the lupus anticoagulant, discrepant results have been obtained with different clotting tests. These have been attributed to various subclasses of LA.⁷⁻¹⁰

Due to its association with diverse disease conditions, the detection of LA is now a part of the laboratory work up of patient with established thromboembolic disorders and recurrent spontaneous abortions in some hospitals.¹¹

Pre-eclampsia is a common obstetric condition in our community. Our aims therefore were to determine the prevalence of LA in women with pre-eclampsia in Benin City, Nigeria and to find out if there is any significant association between pre-eclampsia and L. A.

Patients and Methods

Patients

The study included twenty-six pregnant women (mean gestational age 31 weeks) aged 18 - 45 years who were diagnosed as having pre-eclampsia at the University of Benin Teaching Hospital and fifty apparently healthy pregnant women (mean gestational age 31.7 weeks) aged 18 - 45 years undergoing routine ante-natal clinics.

The patients and controls were recruited into the study having obtained their consents and clearance from the hospital ethic committee.

Methods

Blood Samples

Blood samples were collected by clean venu-puncture into a

clean plastic tube containing 0.129m trisodium citrate in a ratio of one part of anticoagulant to nine parts of blood. Platelet poor plasma were prepared by centrifuging at 2,500g for 15mins at room temperature. The plasma samples were preserved in ice blocks and analyzed within an hour thereafter.

Coagulation tests

The Kaolin clotting time (KCT) was carried out as previously described^{7,8} by pre-incubating 0.2ml of citrated plasma with 0.1ml Kaolin suspension 20g/l in tris buffer (pH 7.4) for 3 minutes at 37°C. The time from the addition of 0.2ml of 0.025m calcium chloride to the formation of a clot was recorded, the procedure was carried out in duplicates for each sample and the average was taken as the clotting time.

Mixing studies were performed using the KCT on prolonged plasma (TP) and normal plasma (NP) in the following proportions of NP/TP 100/0, 80/20, 50/50, 20/80 and 0/100 as earlier described.^{7,8} Plasma from individual healthy volunteers (among hospital staff) with normal coagulation tests were pooled together and used as source of normal plasma. The KCT ratio⁸ 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.⁸

i.e. $\frac{\text{KCT (80\% N: 20\% Test)}}{\text{KCT 100\% N}} \Rightarrow 1.2$

Results

Table 1 shows the KCT values of the twenty-six women with pre-eclampsia and controls. Eleven (42.3%) of the women with pre-eclampsia had prolonged KCT tests. Two (4%) of the pregnant control had prolonged KCT tests, 4(8%) had subnormal KCT whiel 44(88%) had normal KCT. A statistically significant difference between the prevalence of LA in pre-eclampsia (15.4%) and that of pregnant control (2%) p < 0.05 was shown in table 2.

Table 1 KCT values of patients aned controls

| Patient's group | KCT values | | |
|---------------------------------|--------------|---------------|-----------|
| | KCT < 60 sec | 60 - 110 sec. | > 110 sec |
| Pre-eclampsia N = 26 (100) | 2(7.7) | 13(50) | 11(42.3) |
| Pregnant control N = 50(100) | 4(8) | 44(88) | 2(4) |

Percentages in parenthesis
(Normal KCT in our laboratory = 60 - 110 secs)

Table 2 Incidence of LA in pre-eclampsia and controls

| Patient's group | LA | |
|------------------------------|----------|-----------|
| | Present | Absent |
| Pre-eclampsia N = 26(100) | 4(15.4%) | 22(84.6%) |
| Pregnant control N = 50(100) | 1(2) | 49(98) |

Percentage in parenthesis
P < 0.05

Figure 1 shows the graphs obtained from mixing experiments in pre-eclamptics with prolonged initial KCT whose plasma samples were not correctd by mixing with varying proportions of normal plasma. The KCT ratio of all four were greater than 1.2 thus signifying the presence of the lupus anticoagulant. Two of the graphs (p1 and p2), show type 2 patterns which indicate a coagulation factor defect as well as the lupus anticoagulant. While the other two (p3 and p4), show type 3 pattern which indicates the presence of the lupus anticoagulant as well as a cofactor that was needed for its full inhibitory effect⁸.

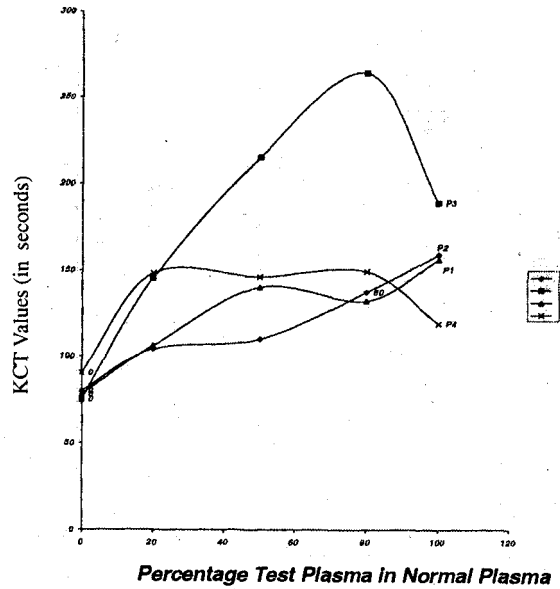


Fig. 1 KCT values of test plasma in various proportion of Normal plasma in preeclampsia (KCT Ratio > 1.2)

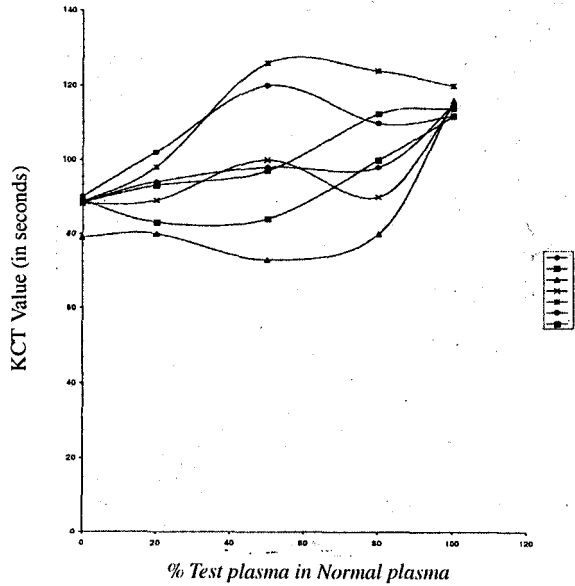


Fig. 2 KCT values of test plasma in various proportions of Normal plasma in preeclampsia (KCT Ratio < 1.2)

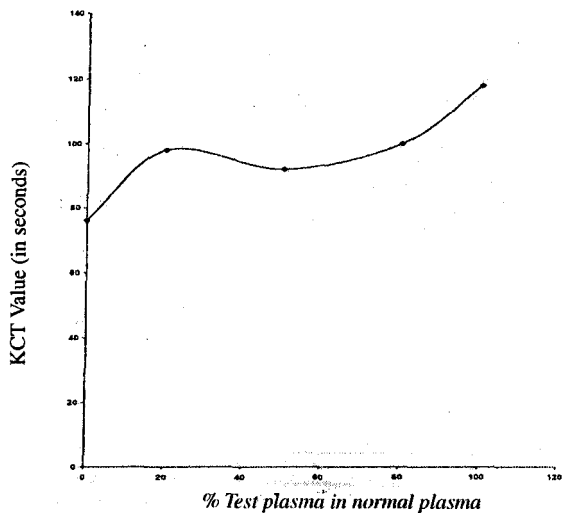


Fig. 3 KCT values of test plasma in various proportion of Normal plasma in pregnant control (KCT Ratio > 1.2)

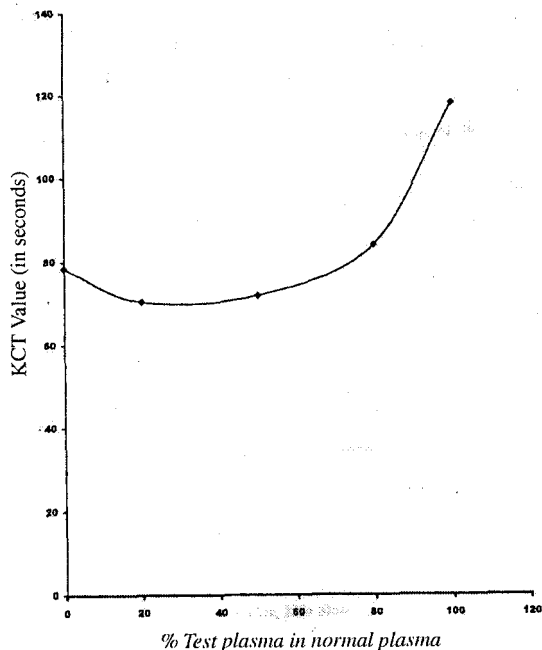


Fig. 4 KCT values of test plasma in various proportion of Normal plasma in pregnant control (KCT Ratio < 1.2)

The graphs obtained for the seven whose prolonged clotting tests were corrected by varying proportions of normal plasma were shown in figure 2. The entire KCT ratios were less than 1.2.

Figure 3 shows the graph of mixing experiments on the pregnant control plasma with prolonged clotting time. The clotting time was not corrected by the addition of normal plasma and the KCT ratio was greater than 1.2, it also shows a type 2 pattern. The addition of normal plasma corrected the prolonged clotting time in a pregnant control plasma (Figure 4). The KCT ratio was less than 1.2 and the graph shows a type IV pattern emphasizing the absence of LA.⁸

Discussion

Despite the widely reported association of the lupus anticoagulant with many clinical conditions in the last decade,^{1,2,3} very little has been heard about it in developing countries like Nigeria. In this study we found a 15.4% prevalence of LA in women having pre-eclampsia. The criteria for diagnosis used in this study i.e. the large proportion of normal plasma (80%) to test plasma (20%) might have eliminated some individuals with weak LA, furthermore the KCT might not have been sensitive to all the isotopes of LA and therefore might have missed some.¹²

The prevalence of 15.4% obtained in this study agrees with a prevalence of 16% reported by Branch et al in the Caucasians^{11,12} suggesting that there is probably no racial variation in the association of LA with pre-eclampsia.

We have also found a statistically significant difference between the prevalence of LA in Pre-eclampsia and apparently healthy women undergoing normal pregnancy ($P < 0.05$). Although, it remains controversial whether LA is causal or consequence of some of the clinical manifestations with which it has been associated,¹³ in women with obstetric complication a better pregnancy outcome

has been reported when the LA was treated with steroids.^{11,12}

A 2% prevalence of LA among apparently healthy pregnant women was obtained in this study. In our centre a prevalence of 8% among non-pregnant multiparous women was observed. It is possible that the LA is masked by normal uncomplicated pregnancy.

We conclude that the prevalence of LA in Pre-eclampsia in Nigeria is quite significant and as such all women with pre-eclampsia in this environment should be screened for LA as part of their normal investigation.

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