

The Lupus Anticoagulant in a Population of Healthy Nigerian Adults

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SUMMARY

Patients with the antiphospholipid syndrome are at a high risk of recurrent thrombosis and recurrent fetal loss. Infertility and a number of other clinical manifestations have also been attributed to this syndrome. There are many tests for detecting the presence of the lupus anticoagulant but the most sensitive remains controversial. In this study we have used a combination of activated partial thromboplastin time (aPTT) and Kaolin clotting time (KCT) to determine the presence of the antibody in 125 healthy individuals which included pregnant women. Six (4.8%) and four (3.2%) of the subjects had elevated aPTT and a KCT ratio ≥ 1.2 respectively. The tests showed a high prevalence of the lupus anticoagulant in the multiparous group than the other groups while there is paucity of the anticoagulant in the pregnant women who are not at risk. We suggest the use of both aPTT and KCT for the screening of patients in whom the antiphospholipid syndrome is suspected.

INTRODUCTION

The lupus anticoagulant (LA) is an immunoglobulin that binds phospholipid and hence inhibits coagulation tests. It is not only found in disease states but could be detected in healthy people [1]. The identification of this antibody is a routine procedure in developed countries but this is not yet so in developing countries and because of this, the diagnosis of the antiphospholipid syndrome is often based on clinical assessment.

The anticoagulant which was first described in association with systemic lupus erythematosus

(SLE) [2] is sought for when a clinician suspects the presence of the inhibitor due to its recognized clinical features or an unexplained prolonged Activated Partial Thromboplastin Time (aPTT). There are various tests available for detecting the presence of the lupus anticoagulant but the most sensitive remains a controversy. The tests used are the aPTT [3], kaolin clotting time (KCT) [4], dilute Russell's viper venom time (RVVT) [5], and the platelet neutralization test (PNT) [6]. At least two of these tests must be performed when investigating a patient suspected of having the lupus anticoagulant [6]. Detection of anticardiolipin antibody using enzyme linked immunosorbent assay is another test which is sensitive to the presence of the anticoagulant but this may not be practicable in a developing country set up.

In this study the presence of the lupus anticoagulant was sought for in healthy individuals using the aPTT and the KCT.

MATERIALS AND METHODS

The population studied included 125 healthy adults comprising 51 male and 74 female. Twenty-six of the females were nulliparous, 25 multiparous and 23 pregnant women with no history of habitual abortion, infertility or eclampsia.

A free flowing venous blood was collected from each subject, 4.5mls of which was delivered into plastic tubes containing 0.5ml of 3.2% trisodium citrate. Platelet poor plasma was prepared by centrifugation of the collected blood at 2000g for 30 minutes. The plasma was processed within two hours of collection. Control plasma was obtained from 6-8 healthy volunteers.

KCT and aPTT were determined by standard methods with bovine brain as the source of phospholipids [7]. A graph was plotted for each

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of the subjects and a KCT ratio determined thus:

$$\frac{\text{KCT (80\%N: 20\%test)}}{\text{KCT 100\%N}}$$

The lupus anticoagulant was taken to be present at a KCT ratio of ≥ 1.2 (8) the graph was interpreted as described by Laffan & Bradshaw [8]:

- Pattern 1 - Classical lupus anticoagulant.
- Pattern 2 - Coagulation factor deficiency as well as lupus anticoagulant.
- Pattern 3 - Plasma containing the anticoagulant but also deficient in a cofactor necessary for its full inhibitory effect.
- Pattern 4 - Absence of lupus anticoagulant.

RESULTS

The ages of the subjects ranged between 19 years and 42 years with a median of 25.5 years. The mean aPTT was 39.8 ± 5.5 seconds and the mean KCT was 82.1 ± 20.4 seconds. Twenty seven (22 %) of the subjects studied had the pattern 1 graph while

54 (43%) and 26(21%) had the patterns 2 and 3 graphs, respectively, only 18(14%) had the Pattern 4 graph (Table I). Four (3.2%) of the population screened had a KCT ratio of ≥ 1.2 and thus could be interpreted as having the lupus anticoagulant; all these were males and had the pattern 2 graph. Table II shows the relationship between the PTTK and KCT of each group with the pattern of the graph obtained.

aPTT that was greater than 50 seconds (mean $\pm 2SD$) was taken as abnormal. This was seen in 6(4.8%) of the subjects studied, this comprised 2(1.6%) of the males, 1(0.8%) pregnant woman and 3(2.4%) of the multiparous women. None of the nulliparous females had a value greater than 50 seconds.

DISCUSSION

The term lupus anticoagulant (LA) is a misnomer since it is associated with thromboembolic disorder

TABLE 1: Prevalence of the different LA graph patterns in the different groups.

Type of LA graph	Study population	Male	Pregnant female	Multiparous female	Nulliparous female
1	27(21.6%)	14(27%)	0	11(44%)	2(8%)
2	54(43.2%)	24(47%)	11(47%)	6(26%)	13(50%)
3	26(20.8%)	10(20%)	6(26%)	5(20%)	5(19%)
4	18(14.4%)	3(6%)	6(26%)	3(12%)	6(23%)

TABLE 2: The relationship between the mean PTTK and KCT of each group with the type of graph obtained.

Types of graph	Males		Pregnant Females		Multiparous Females		Nulliparous females	
	PTTK	KCT	PTTK	KCT	PTTK	KCT	PTTK	KCT
Type 1	38.1	80.1	-	-	42.0	81.5	40.0	93.0
Type 2	41.7	98.9	41.7	73.3	45.0	102.8	39.6	89.7
Type 3	36.7	67.6	36.0	74.8	39.6	75.5	36.5	59.5
Type 4	34.6	65.0	40.0	79.7	36.0	70.3	37.7	83.0

rather than a bleeding tendency. It is known to occur in a variety of conditions and particularly in obstetrics cases where adverse effects like early abortions and second or third trimester intrauterine deaths are common. Successful pregnancies do however occur in the presence of the lupus anticoagulant[6]. The prevalence of the anticoagulant among women with a history of two or more miscarriages varies between 5-50% in different series [9]; the prevalence in SLE may be as high as 65%. In this study of normal subjects, 21.6% had the classical lupus graph, the use of the KCT ratio however brought the prevalence down to 3.2%, which is similar to a prevalence of 2.3%, found in the sera of pregnant primiparous women in an antenatal clinic in West Indies [10]. The subjects studied are in the reproductive age group because this is the age group in whom the obstetric complications of the lupus anticoagulant are most likely to be encountered.

Inter-laboratory variations exist in detecting the antiphospholipid antibody particularly in the detection of the anticardiolipin antibody. In contrast, lupus anticoagulant results are more reproducible despite the fact that these tests are laborious[11]. The detection of the lupus anticoagulant will require the use of more than one test, with the aPTT as a screening procedure [12]. There is therefore the need for at least one other method in excluding the anticoagulant. No significant difference was found in specificity among aPTT, dRVVT, KCT and dilute aPTT but aPTT and dRVVT were significantly more specific than anticardiolipin antibodies [13]. Dilute aPTT was found to be more sensitive than dRVVT, KCT and aPTT. It is therefore recommended that the aPTT be used as a screening procedure for LA and the KCT, dRVVT or dilute aPTT be used for confirmation in laboratories that cannot afford procedures that are more sophisticated.

It is surprising that the pattern 1 graph that typifies the classical lupus anticoagulant was not recorded among the pregnant females; they also had the highest prevalence of the pattern 4 graph (No LA). More of the pregnant women however had the pattern 3 graph. The presence of more of the pattern 3 graph in the pregnant women compared to the other groups might explain why the lupus anticoagulant is implicated in many obstetrics condi-

tions, since the cofactor which is necessary for the full inhibitory effect of the anticoagulant is low among them. The multiparous women on the other hand recorded the highest prevalence of the pattern 1 graph and a low prevalence of the pattern 4 graphs. The mean PTTK and KCT of this group are also higher than those of the other groups. This could be why 90% of cases of SLE are seen in women and usually in the childbearing age. The presence of the lupus anticoagulant (in its different forms) in 86% of the population in this study will explain its association with a variety of diseases. There is however, a need for further studies using these tests on patients who are at risk of having the lupus anticoagulant.

We conclude that a combination of the aPTT and the KCT ratio will suffice in confirming the diagnosis of the lupus anticoagulant in a developing country.

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