LUPUS ANTICOAGULANT IN INTRAUTERINE FETAL DEATH

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SUMMARY

The objective of this prospective clinical study was to determine the association of Lupus Anticoagulant (LA) in unexplained intrauterine fetal death (IUFD). One hundred pregnant women with unexplained intrauterine fetal death in the current or past pregnancy and an equal no. of control women with no history of adverse pregnancy outcome were recruited. LA was detected by finding an abnormal Kaolin clotting time index. The difference in the presence of LA between the two groups was analysed by use of Chi Square test. LA was detected to be present in only two of the study subjects. These women presented with an IUFD in this pregnancy and had late second trimester abortions in their previous pregnancies. None of the controls tested positive for LA. Lupus anticoagulant when present in the circulation of a pregnant woman is a strong predictor of fetal demise as none of the pregnancies in the LA positive women culminated in a live birth.

INTRODUCTION

Intrauterine fetal death (IUFD) is related to a number of maternal and/or fetal factors and in about a fifth of cases no definite reasons can be given and traditional evaluation for this fetal loss yields no positive factor (Donald 1979). Recently autoimmune factors have been recognised to be responsible for recurrent pregnancy losses (Dudley et al 1989). In women with SLE the rate of IUFD ranges from 11.2% to 46.2% in a study by Junco in 1986. In

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Accepted for Publication on May 96

these patients the presence of antiphospholipid antibodies such as Lupus Anticoagulant (LA) and Anticardiolipin antibodies (ACA) have been proven to be a strong predictor of fetal distress and demise (Lockshin et al 1985).

LA and ACA have been linked to adverse pregnancy events and recently these antibodies have been observed in the plasma from patients with non SLE related disorders as well as in those with no clinically diagnosed autoimmune disease. According to Hadi & Treadwell (1990) placental thrombosis and infarction in the presence of antiphospholipid antibodies is believed to play a major role in the pathogenesis of these adverse pregnancy events.

Various studies have found a high incidence of spontaneous abortions and fetal death in women positive for LA (Lubbe et al 1984, Branch et al 1985). The aim of this study was to find the role of AL if any, in women with unexplained intrauterine fetal death.

MATERIALS AND METHODS

The study was conducted in the department of Obstetrics and Gynaecology, Nehru Hospital attached to the Postgraduate Institute of Medical Education and Research, Chandigarh, India in the period July 1992 to May 1993. A total of two hundred pregnant subjects were recruited for this study. Study group comprised of 100 subjects, 85 of whom experienced an IUFD in a previous pregnancy and 15 had IUFD in current pregnancy, for which no cause could be identified despite intensive investigations. Control group comprised of 100 subjects who had a normal live birth preceding this pregnancy with no history of previous fetal wastage either early or late.

All the pregnant women were regularly supervised in the antenatal clinic and high risk pregnancy clinic as necessary. They were subjected to a thorough general physical and obstetrical examination. All investigations required to find the cause of intrauterine deaths were done. Blood sample for LA was taken between 20-24 weeks of gestation. In the group with IUFD in the current pregnancy, after ruling out other causes of fetal death blood sample for LA was taken at the time of their admission to the labour room.

The factor LA prolongs the phospholipid dependent coagulation tests in vitro and causes thrombosis in vivo. Platelet poor plasma was utilized for the coagulation tests. The prothrombin time (PT) and partial thromboplastin time with Kaolin (PTTK) was recorded for all subjects by the standard laboratory procedures (Daci & Lewis, 1991). LA was detected using the kaolin clotting time (Exner et al; 1978) from which the Kaolin clotting time index (KCT Index) was estimated. KCT index > 15 signified the presence of LA in a given blood sample (Rosner et al, 1987). Statistical analysis was done using the Chi square test.

RESULTS

Subjects were comparable with respect to age, with higher gravidity in the study group as expected. The data regarding past obstetrical performance of the study subjects is presented in Table I. These women had experienced a total of 169 pregnancies in the past of which only 33 (19.5%) ended in live births. 39 (23%) were lost as abortions

Table I
OUTCOME OF PREVIOUS PREGNANCIES IN STUDY GROUP

Total number of pregnancies		169
Live births	33	
Abortions :		
First trimester	18	
Second trimester	21	
IUFD :		
Preterm	39	
Term	58	

Table II
LUPUS ANTICOAGULANT POSITIVITY

Lupus Anticoagulant	Study Group	Control Group
Positive	2	0
Negative	98	100

$X_2 = 0.656$; $P>0.05$

and 97 (57.3%) had ended in third trimester IUFD. In the control group all previous pregnancies had ended in live births.

The results of PT and PTTK did not differ significantly in the two groups.

In the study group LA was detected in only 2 subjects and none of the controls tested positive for LA. This difference was found to be statistically insignificant (Table II). Both the LA positive women had attended the hospital with an IUFD in the early third trimester in the present pregnancy and had earlier aborted dead fetuses in late second trimester in their previous pregnancies as well.

In the present pregnancy of control group women, all but one subject had live births. The only stillbirth that occurred was due to transverse lie with hand prolapse.

Table III shows the outcome of present pregnancy in LA positive and negative subjects in the study groups. Of the 98 pregnancies in LA negative women 82 (83.6%) ended in live births, one presented as missed abortion and 15 (17.3%) ended as IUFD. As compared to this, there were no live births in LA positive subjects and this is statistically significant. In the positive

Table III
OUTCOME OF PRESENT PREGNANCY IN LA POSITIVE AND NEGATIVE SUBJECTS IN THE STUDY GROUP

	Lupus Anticoagulant	
	Negative	Positive
Total Pregnancies	98	2
Live births	82	0*
Missed abortion	1	0
IUFD		
Preterm	11	2
Term	4	0

*X_2 = 4.492 $p<0.05$

group both pregnancies ended as preterm IUFD. This signifies that LA in a pregnant woman is associated with a definite increased risk of fetal demise.

Majority of women (70%) with previous bad obstetrical history had elective induction of labour. There was a higher incidence of caesarean section in the study group (24%) as compared to the control group (18%). Furthermore 17% of the subjects in the study group developed acute fetal distress against only 5% of the controls, indicating study group to be at an increased risk for the development of intrapartum fetal hypoxia.

DISCUSSION

Among the women who attended High Risk Pregnancy clinic of our institute with history of IUFD, no cause can be ascertained for the pregnancy loss in nearly 35-40% of the cases. Recently immunological factors have been implicated to be playing role in pregnancy losses. Carreras et al (1981) had discovered LA in 2 out of 24 women with history of repeated abortions, intrauterine growth retardation and intrauterine death of unknown origin. Lockwood et al in 1989 studied the prevalence of LA in a low risk obstetrical population and found it to be only 0.2%. This study tried to find the association, if any, of LA with obstetrical performance especially in women with unexplained IUFD in the present or current pregnancy.

In this study only 2 out of 100 subjects with unexplained IUFD in previous/current pregnancy were found to be positive for circulation LA. None of the controls tested positive for LA and the difference was not statistically significant.

The two women who tested positive for LA were amongst the fifteen woman who presented with an IUFD in their current

pregnancy. These LA positive women had in their preceding pregnancies aborted in late second trimester death fetuses with no apparent malformations. Again in their current pregnancies they presented to the hospital with IUFD in early third trimester, for which no causative factor was found except for the presence of circulating LA.

No live births occurred in LA positive subjects and this was statistically significant when compared with 97-99% live birth rate in subjects who tested negative for LA. This concludes that though LA might not be a significant etiological factor in the genesis of pregnancy loss, its presence in a pregnant woman is associated with a significant risk of fetal demise especially in late second and early third trimester. Treatment with prednisolone and aspirin has been advocated to improve pregnancy outcome of these patients. Hence, LA being a treatable cause of fetal death, the presence of this autoantibody should be sought for in subjects with unexplained fetal loss.

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