PREVALENCE OF LUPUS ANTICOAGULANT IN PREGNANCY HYPERTENSION AND ITS SIGNIFICANCE ON PREGNANCY OUTCOME

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SUMMARY

One hundred and seven cases with pregnancy hypertension and 50 normally pregnant women were studied for lupus anticoagulant activity. Lupus anti-coagulant was present in 14.1% cases of pregnancy hypertension. It was almost equally distributed in gestational hypertension (17.7%) and pre-eclampsia (12.9%)/ Incidence was more in severe (25%) than in moderate (17.1%) and mild (9.3%) hypertension. Incidence of thrombocytopenia was higher (33.3%) in positive cases than in negative cases (9.8%) which is statistically significant (P <0.05). False positive VDRL serology was significantly higher (20%) in positive than in negative mothers (P <0.01). LSCS rate was much higher (33.3%) in hypertensive cases positive for lupus anticoagulant than in negative cases (19.6%). The mean birth weight of the neonates was 1881.3 gms and 2555.0 gms born to positive and negative mothers respectively. Perinatal mortality was higher (38.8%) in positive mothers, mainly due to low birth weight which was seen in 55.5% against 15.2% in negative mothers (P <0.01). Hence lupus anti-coagulant activity should be determined in pregnancy hypertension.

INTRODUCTION

The Lupus anti-coagulant, an acquired immunoglobulin, mostly IgG is a phospholipid dependant coagulation inhibitor (Lechner - 1974). Although first observed in patients of systemic Lupus erythematosus, subsequently it was found that besides other clinical conditions, it is associated with major obstetric complications, such as

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recurrent foetal loss, intra-uterine growth retardation and pre-eclampsia (Branch et al 1985), Clauvel et al - 1986, Deruc et al - 1985, Lubbe et al - 1984, Rafla & Farquharson - 1991 and Sletnes - 1991). Lupus anti-coagulant inhibits the prostacyclin release from the vessel wall and interacts with the phospholipid fraction of the platelets to predispose for placental thrombosis and infarction (Henk et al - 1991) which is responsible for prolonged foetal hypoxia and thus causes intra-uterine growth retardation. A successful pregnancy outcome has been reported when immuno-suppressive therapy either with prednisolone/and aspirin (Lubbe et al - 1983) or I.V. immunoglobulin infusion (Katz et al - 1990) is used to inhibit lupus anti-coagulant is an identifiable and treatable cause of major pregnancy complications, not much work has been reported in Indian Obstetric population. This study was undertaken to determine the prevalence of lupus anti-coagulant in pregnancy complicated with hypertension and it's relationship to foetal outcome.

MATERIAL & METHODS

In this prospective study, 157 pregnant mothers during third trimester were screened for lupus anti-coagulant (LAC) over a period through Sept '1993 to May '1994. This study was approved by the ethical committee of the institution. These cases were divided into two groups, study group which consisted of 107 cases of pregnancy hypertension and control group comprised of 50 normally pregnant women. Hypertension was diagnosed when the BP was >140/90 mmHg on at least two occasions with an interval of 6 hours and when the period of gestation was >20 weeks. According to the severity of hypertension, cases were distributed into mild, moderate and severe. These women were placed into specific groups, according to the type of hypertension. In the control group, the women were normotensive, with singleton pregnancy, gestation >37 weeks to 40 weeks and when there was no past history suggestive of BOH, autoimmune disorder, thromboembolic phenomenon, thrombocytopenia or drug intake which could have produced lupus like antibodies. Any clinical evidence of IUGR was excluded in these cases. Cases were clinically evaluated and routine laboratory tests were done, complete haemogram with peripheral smear to exclude any evidence of haemolysis, urine analysis, KFT, LFT, VDRL, Random Blood sugar levels, blood group and Rh typing, were done to exclude other causes of adverse foetal outcome.

Standard coagulation tests were performed which included Prothrombin time (PT), activated partial thromboplastine time (APTT) and Thromboplastin Time (TT) to exclude any coagulation disorder. Lupus anti-coagulant was assessed by performing PTT-LA (Stago-Italy). In lupus anti-coagulant positive cases, other tests such as estimation of fibrinogen levels, presence of heparin, intrinsic pathway factor deficiency and presence of factor inhibitors were performed, to exclude other causes of prolonged PTT-LA. Neonate born was labelled intra-uterine growth retarded, if the birth weight was less than 10th percentile of the average weight for that period of gestation. Lupus anti-coagulant activity was correlated with the type of hyperten-

sion, grade of hypertension and the pregnancy outcome.

OBSERVATIONS & RESULTS

The mean age in the control group & the study group was comparable, 24.5 years (17-30 yrs) and 23.1 years (18-36 yrs.) respectively. In control group, 22 (44%) mothers were primigaida, the mean diastolic/Blood pressure was 75 mm of Hg, mean platelet count was 169.5 thound/mm3 (Range 61-343 thound/mm3). Thrombocytopenia was seen in 5 (10%) cases. False VDRL positive serology was seen in 1 (2%) cases. Mean gastational age at delivery was 38.5 weeks (>37 weeks to 40 weeks). Fourty-eight (96%) women had normal vaginal delivery and in 2(4%) delivery was assisted with forceps. All the babies born were live births. Mean birth weight was 2790.2 gms & 7(14%) were low birth weight babies. In 3 (6%), babies had respiratory distress at birth, which could be treated successfully.

Of 107 mothers with pregnancy hypertension, 15 (14.1%) were positive for lupus anti-coagulant. In the control group, none of the patient was found positive & this

Table I

Distribution of 15 cases with Lupus anti-coagulant activity according to the type of hypertension and grade of hypertension.

Hypertensive Cases (n=107)	LAC + ive (n=15)		LAC -ve (n=92)	
	Pt.No	(%)	Pt.No	(%)
I. Type of Hypertension				
1. Gestational Hypertension (n=45)	8	(17.7)	37	(82.2)
2. Pre-eclampsia (n=54)	7	(12.9)	47	(87.1)
3. Eclampsia (n=3)	0	(0)	3	(100)
4. Chronic Hypertension (n=5)	0	(0)	5	(100)
II. Grade of Hypertension (Diastolic B.P./mmHg				
1. Mild (n=54) (90-100)	5	(9.3)	49	(90.7)
2. Moderate (n=41) (100-110)	7	(17.1)	34	(82.9)
3. Severe (n=12) (110 and above)	3	(25%)	9	(75%)

Severe hypertension was more frequent in cases positive for Lupus anti-coagulant.

Table II
Summary of Pregnancy hypertension cases (N=107) In Relation to Lupus anti-coagulant activity.

Clinical Characteristics	LAC + VC (N=15)	LAC - VC (N=92)	Statistical Significance
1. Mean Age (Years)	24.5	23.1	-
2. Gravidity			
- Primigr	60%	54.4%	NS
- Multigr	40%	45.6%	
3. H/O BOH	3 (20%)	16 (17.3%)	NS
4. Mean Diastolic B.P. (mmHg)	97.0	95.0	-
5. VDRL reactivity (False - Positive	3 (20%)	2 (2.2%)	P <0.01
6. Thrombocytopenia	5 (33.3%)	9(9.8%)	P <0.05
7. Mean gest age (Wks) at delivery	36.6	38.5	-
8. Operative delivery (LSCS -Rate)	5 (33.3%)	18 (19.6%)	NS
9. Mean Birth Wt. (gms)	1881.3	2555.0	-
10. Still-birth rate	2 (11.1%)	6 (6.5%)	NS
11. IUGR	10 (55.5%)	14 (15.2%)	p < 0.01
12. Neonatal Mortality	5 (27.7%)	5 (5.4%)	P < 0.01

difference was statistically significant (P <0.01). In respect to the type of hypertension 8 (17.7%) out of 45 cases of gestational hypertension & 7 (12.9%). Out of 54 cases of pre-eclampsia were positive for lupus anti-coagulant activity. In relation to the severity of hypertension lupus anti-coagulant was more frequently seen in severe 3 (25%) of 12 than moderate 7 (17.1%) of 41, to mild 5 (9.3%) of 54 cases of hypertension (Table I). Incidence of mild to moderate thrombocytopenia was noted in 5 (33.3%) against 9 (9.8%) in LAC positive & negative mothers respectively & this difference was statistically significant (P<0.05). False positive VDRL serology was noted in significantly higher number of mothers, present in 3 (20%) against 2 (2.2%) in LAC positive and negative mothers respectively (P <0.01) (Table II).

In LAC positive mothers 60% (9 out of 15) whereas in LAC - ive mothers 54.4% (50 out of 92) were primigravida. History of previous pregnancy losses was present

Table - III
Distribution of 18 Neonates born to LAC + VC and LAC Negative mothers according to their birth weight

Patient Group	Birth Weight (gms)			Mean birth Wt.(Gms.)
	< 2000 Pt.No.(%)	2000-2500 Pt.No.(%)	> 2500 Pt.No.(%)	
1. Control (N = 50)	0 (0)	7 (14)	43 (96)	2790.2
2. Study (N-107)				
- LAC - VC (N = 92)	14 (15.2)	14 (15.2)	64 (68.6)	2555.0
- LAC + VC (N = 18)*	10 (55.5)	5 (22.2)	4 (22.2)	1881.3

* One woman gave birth to quadruplets

in 66.6 (4 out of 12) in positive cases against 35% (26 out of 92) in negative mothers. Mean diastolic blood pressure was 97mm of Hg against 95 mm of Hg in LAC positive & negative mothers respectively. False positive VDRL serology was significantly higher, present in 3 (20%) LAC cases against 2 (2.2%) LAC negative mothers. ($P < 0.01$). All other haematological investigations were with in normal limits in both LAC positive & LAC negative hypertensive mothers. The mean gestational age at delivery was lower (36.6 weeks) in LAC positive mothers compared to 38.5 weeks in LAC negative mothers. The caesarean section rate was higher in LAC positive mothers, seen in 5 (33.3%) deliveries compared to 18 (19.6%) in LAC negative mothers. Major indication for LSCS in positive mothers was foetal distress, present in 4 (80%) cases intra-partum (3) ante partum (1). On the other hand, LSCS was done in LAC negative mothers for foetal distress in 9 (50%) cases only. The mean birth weight was 1881.3 gms and 2555.0 gms in positive & negative hypertensive mothers respectively (Table-III).

Of 18 babies born to LAC positive mothers 14 (77.7%) were low birth weight and in 10 (55.5%) the birth weight was less than 2000 gms. Conversely, in LAC negative hypertension cases, only 14 (15.2%) babies were low birth weight & this difference in birth weight was statistically significant ($P < 0.001$). Although, the still-birth rate in positive and negative mothers was not very different as seen in 2 (11.1%) and 6 (6.5%) respectively. The neonatal death rate was much higher in LAC positive cases seen in 5 (27.7%) against 5 (5.4%) in LAC negative & this difference was statistically significant ($P < 0.01$). Neonatal morbidity was significantly higher in LAC positive,

Table IV
Foetal Outcome at delivery and in the neonatal period

Foetal Outcome	Study Group (N=107) LAC+VC (N=18)* Pt.No. (%)		LAC-VC (N-92) Pt.No. (%)		Control Group (N=50)	
1. Live Birth	16	(88.8)	86	(93.5)	50	(100)
2. Still-Birth						
- Term	2	(11.1)	4	(4.3)	-	-
- Preterm	0	(0)	2	(2.2)	-	-
3. Neonatal Complications						
- RDS**	2	(11.1)	7	(7.6)	3	(6)
- MAS***	1	(5.6)	3	(3.3)	0	(0)
- LBW****	10	(55.5)	14	(15.2)	7	(14)
4. Neonatal mortality						
- Term	4	(22.2)	3	(3.3)	0	(0)
- Preterm	1	(5.6)	2	(2.2)	0	(0)

The perinatal loss in lupus anti-coagulant was (38.9%). Neonatal morbidity was noted in 13 (72.2%), when it was only in 24 (26%) LAC negative mothers with hypertension and 10 (20%) in control group.

* One woman LAC positive gave birth to quadruplets.

** Respiratory Distress Syndrome

*** Meconeum Aspiration Syndrome

**** Low Birth weight

seen in 13 (72.2%) compared to LAC negative cases, noted only in 24 (26% cases. Sixteen (88.8%) out of 18 babies were born alive in LAC positive mothers & 86 (93.5%) were live births in LAC negative mothers. Hence the incidence of live births was similar in both the groups but the total foetal loss (38.8%) consisting of still-birth (11.1%) & neonatal death rate of 27.7% was much higher in LAC positive hypertensive mothers (Table-IV).

DISCUSSION

Increased prevalence of lupus anti-coagulant activity has been reported in cases of pregnancy complicated with hypertension, with an incidence of 16% (Branch et al - 1985, Rafla and Farquharson - 1991 and Milliez et al - 1991). In this study also a comparable incidence of 14.1% was observed in cases of pregnancy hypertension. Inhibition of prostacyclin production mediated by the Lupus anti-coagulant activity

may explain the high rates of pre-eclampsia and foetal growth retardation observed in these mothers. Scott (1987) could not establish any association between lupus anti-coagulant activity and pre-eclampsia in his series. As noted in this study and reported earlier, the incidence of lupus anti-coagulant was equally distributed in cases of gestational hypertension (17.7%) and pre-eclampsia in (12.9%). Lupus anti-coagulant is more commonly associated with severe hypertension (25%), than in moderate (17.1%) to mild (9.3%) & similar observations have been made by Branch et al - (1985) & Lubbe et al - (1984). However, Milliez et al - (1991) did not observe any difference in the incidence in relation to the severity of hypertension. History of previous pregnancy loss noted in 66.6% cases in our series is much lower than the incidence of 94% to 96.8% pregnancy loss reported by earlier authors (Branch et al - 1985) & Lubbe et al - (1984).

Thrombocytopenia is a common finding in patients with lupus anti-coagulant activity & in the present study also it was 3 times more common (33.3%) than in lupus anti-coagulant negative cases seen in 9.8% (Elias & Elder - 1984 & Love & Santaro - 1990). Increased incidence of false positive VDRL reactivity is seen in lupus anti-coagulant positive cases. It was noted in 20% of cases in the present study and love & Santoro (1990) have also reported an incidence of 47% in a series of 319 cases positive for lupus anti-coagulant in their study.

The mean gestational age was lower (36.6 weeks) & the same has been reported by Rafla & Fanquharson (1991) and they have reported a mean gestational age of 35 weeks in their series. A higher incidence of caesarean section rate (33.3%) mainly done for foetal distress (80%) as observed in this study is comparable to an incidence of LSCS of 43% observed by Rafla & Fanquharson (1991). The high incidence of intrapartum foetal distress in these cases may be attributed to the prolonged antepartum foetal hypoxia, because of the placental in sufficiency as a result of increased infarction & placental necrosis induced by lupus anti-coagulant. Intrauterine growth retardation is most common clinical manifestation noted in cases, positive for lupus anti-coagulant in pregnancy (Rafla & Fanquharson-1991). In our study also intrauterine growth retardation was observed in 77.7%, of which 55.5% were severely retarded babies. Although the still-birth rate was only 11.1% this study comparable with the still-birth rate of 12% reported by Lockwood (1989), the total perinatal loss (38.8%) was significantly higher in these cases. The increased neonatal mortality & morbidity is mainly contributed by the low-birth-weight due to intrauterine growth retardation (McCormick - 1985). In our study also, the neonatal morbidity was 4 times more in lupus anti-coagulant positive cases than in lupus anti-coagulant negative cases of pregnancy hypertension.

CONCLUSION

From the results noted in this study, it can be suggested that lupus anti-coagulant should be determined in pregnancy complicated with hypertension and when there is a previous history of poor pregnancy outcome.

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