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Fetal cord serum prolactin (PRL) levels in normal and abnormal pregnancies and its relation to development of RDS

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Abstract
Lower cord blood serum prolactin levels in fetus is considered as one of the major contributor for the development of respiratory distress syndrome (RDS) in newborns considerably in high risk pregnancies. Along with other hormone parameters like estradiol, cortisol, testosterone, thyroid hormones, glucagon and insulin; prolactin PRL is one of the hormone that plays a role in fetal lung maturation. Cord serum prolactin (PRL) was directly proportional to gestational age in normal and abnormal pregnancies, irrespective of their maternal age, parity, socioeconomic status, geographical background and mode of delivery. Women with abnormal (high risk) pregnancies had significantly lower (285.01+/-54.474vs376.34+/-100.309 ng/ml) prolactin level as compared to that with normal pregnancy. Women with lower PRL levels had higher incidence of babies with RDS as compared to women with higher PRL levels. We conclude from our study that low cord blood serum prolactin levels were strongly associated with adverse neonatal outcome.

Keywords: Cord blood serum prolactin, respiratory distress syndrome, high risk pregnancies, lung maturation

Introduction
Hyaline Membrane disease (HMD) is the most common cause of Respiratory Distress Syndrome (RDS) leading to mortality / morbidity in preterm babies [2]. Adequacy of lung surfactants ensures alveolar stability that is required to establish effective ventilation at the time of first breath [1]. Several hormones (estradiol, cortisol, testosterone, thyroid hormones, glucagon, and insulin) are responsible for the production of lung surfactants. Prolactin in increasing concentration through a complex mechanism seems to participate in pulmonary maturation [1, 2].
It has been demonstrated from studies that surfactant is mainly constituted of 90% lipids and 10% proteins. Phospholipids form the bulk of lipids present in the surfactant. Phosphatidylcholine (PC) is the prime phospholipid with surface active properties that makes about 70-80% of the total lipids. It may be present in unsaturated form (17%) or in saturated form (50% with dipalmitoyl species). Phosphatidylglycerol (PG) accounts for about 7% and is the next most abundant lipid which is important for even spreading of the surfactant monolayer on the surface of alveoli (PC as such has very less spreading properties). Prolactin increases phospholipid content of the surfactant specifically Phosphatydylcholine and Phosphatydylglycerol [3].
The nature of this study was to find out the levels of prolactin (PRL) and its role in the development of Respiratory Distress Syndrome (RDS) in normal and high risk pregnancies [Premature labour, Premature rupture of membrane (PROM), Pregnancy induced hypertension, Gestational Diabetes Mellitus (GDM), Intrauterine growth restriction (IUGR) and Anaemia.

Materials and Methods
In this study, 50 pregnant women were divided into two groups: Group A (25 patients) included all normal pregnant women whereas Group B (25 patients) included all abnormal or high risk pregnancies. Certain parameters were noted like gestational age at the time of delivery, mode of delivery, Apgar score at 1st and 5th min, birth weight, and cord blood serum PRL levels. The serum was separated from the cord blood sample and quantitative analysis of serum prolactin was carried out by Lee Bead Prolactin Enzyme Immunoassay.
Neonatologist resuscitated the newborn. The baby was said to have respiratory distress (RDS) according to Downes score for Term neonates and Silvermann Anderson Score for Preterm neonates. Without squeezing the cord, 3ml of mixed umbilical arterial and venous blood was collected in a plain vial just after delivery of the newborn. Sample was kept at room temperature

Results

In this study, mean prolactin of group A (normal pregnancy) was 376.34 ng/ml with standard deviation of 100.309 ng/ml and of group B (high risk pregnancy) was 285.01 ng/ml with standard deviation of 54.474 ng/ml, with P value less than 0.001 (Table 1)

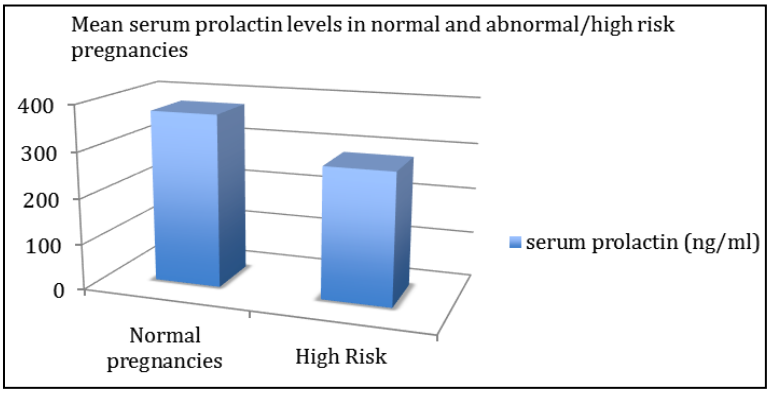

Chart 1. Suggests that mean serum prolactin levels in high risk pregnancies is on a lower side compared to normal pregnancies

Table 1. Co-relation of cord serum prolactin levels in normal and abnormal / high risk pregnancies (*P*<0.001)

Groups	No.	Fetal cord serum PRL Mean (ng/ml)	SD	Std. Error Mean
Normal	25	376.34	100.30	20.062
Abnormal	25	285.01	54.474	10.895

Table 2 shows co-relational of cord serum prolactin levels with normal and abnormal pregnancies and respiratory distress in each group. The mean prolactin levels in group A was 376.34ng/ml with standard deviation of 100.309ng/ml. In group a only 1 baby had respiratory distress and needed NICU admission. Mean prolactin levels in group B was 285.01ng/ml with standard deviation of 54.474ng/ml. In group B, out of 25, 15 babies had respiratory distress with relatively lower level of foetal cord serum prolactin levels. Foetal cord serum prolactin levels in women who were anaemic was around 278.01ng/ml, women with GDM had values of 285.00 ng/ml.

Women who presented in preterm labour had foetal cord serum prolactin levels of 263.25 ng/ml and with premature rupture of membranes, levels were around 303.50 ng/ml. Whereas women who presented in preterm labour with premature rupture of membranes (PROM), foetal cord serum prolactin levels were very low 220 ng/ml. 5 babies out of 8, amongst the preterm group had respiratory distress whereas 3 babies out of 6 had respiratory distress in women who had premature rupture of membranes at term. None of the preterm patients received steroids since they presented in active labour

Table 2. Correlation of cord serum prolactin level with normal and abnormal pregnancies and RDS babies.

	No	%	Prolactin level Mean +/- SD (ng/ml)	No. of RDS babies
Women with normal pregnancy	25	100	376.34 +/- 100.309	1
Women with high risk pregnancy	25	100	285.01 +/- 54.474	15
Anaemia	2	8	278.10 +/- 49.356	
Gestational diabetes mellitus	2	8	285.00 +/- 49.497	2
Intrauterine growth restriction	3	12	330.00 +/- 50.744	2
Pregnancy induced hypertension	2	8	321.00 +/- 115.966	1
Preterm	8	32	263.25 +/- 45.364	5
Premature rupture of membranes	6	24	303.50 +/- 41.176	3
Preterm with PROM	2	8	220.00 +/- 42.426	2
Total		100		

Table 3. Co-relation of fetal cord serum prolactin levels with gestational age in group a (normal pregnancy)

Gestational Age (in weeks)	No. of women	Mean fetal cord serum PRL(ng/ml)	Std. Deviation
37-42	25	376.34	100.309

Table 4. Co-relation of foetal cord serum prolactin levels with gestational age in group B (High Risk Pregnancy) *P*<0.001

Gestational Age (In weeks)	No. of women	Mean fetal cord serum PRL (ng/ml)	SD
30-32	1	190.00	
32-34	4	226.00	30.638
34-37	7	300.71	51.794
37-42	13	302.02	44.595

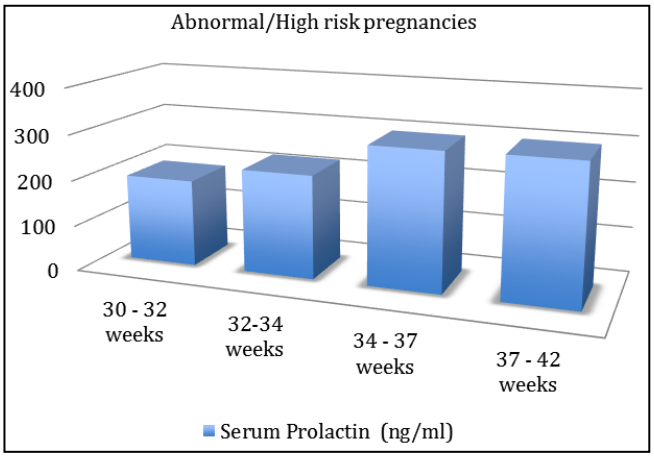

Chart 2. Suggests that serum prolactin levels are directly proportional to gestational age.

In group A, all women were between 37 and 42 weeks of gestation. Mean fetal cord serum prolactin levels in group A was 376.34 ng/ml whereas in group B there was significant increase in the prolactin levels as the gestational age increased. There was only 1 case between 30 to 32 weeks gestation with prolactin levels of 190ng/ml. 4 cases between 32 to 34 weeks with mean serum prolactin levels of 226 ng/ml. 7 cases between 34 to 37 weeks gestation with mean serum prolactin levels of 300.71 ng/ml and 13 cases between 37 to 42 weeks gestation having mean serum prolactin levels of 302.02 ng/ml. As we see in table 3 and 4 there was a steady rise in prolactin levels with gestational age.

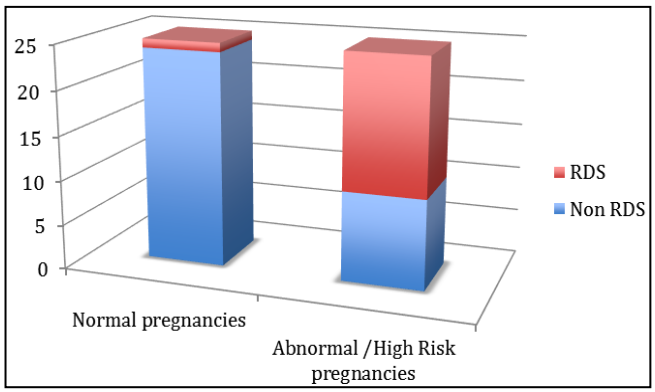

Chart 3. Suggests number of RDS was on a higher side in Abnormal/High risk group

Table 5. Co-relation of cord serum prolactin with birth weight.

Birth wt (gm)	Groups	No. of babies	Fetal cord Serum PRL Mean (ng/ml)	SD
<1500	Abnormal	2	188.00	2.828
1500-2499	Normal	4	434.93	97.076
	Abnormal	14	301.93	56.614
>2500	Normal	21	365.18	99.214
	Abnormal	9	280.24	28.523

Table 6. Cord serum prolactin levels in RDS and non-RDS babies

Group	Respiratory distress	No. of babies	Mean fetal cord Serum Prolactin (ng/ml)	Std. Deviation
Group A Normal Pregnancy	No	24	381.06	99.587
	Yes	1	263.00	
Group B Abnormal/ High risk Pregnancy	No	10	304.92	50.678
	Yes	15	271.73	54.442

Out of 50 babies, 30 babies weighed above 2500gm, where 21 babies were from group A having mean serum prolactin levels of 365.18 ng/ml and 9 babies were from group B having mean serum prolactin of 280.24 ng/ml which was relative to a lower side compared to group A. 18 babies weighed between 1500gm to 2499gm. Out of 18, 4 babies were group A having mean prolactin level of 434.93 and 14 babies were from group B having mean serum prolactin level of 301.93ng/ml. And only 2 babies weighed below 1500gm having mean serum prolactin level of 188.00 ng/ml. From table 5, it is evident that serum prolactin levels were high in group A than group B when categorized according to their birth weights.

In table 6, it is evident that in group A out of 25 babies, only 1 baby had respiratory distress with serum prolactin level of 263 ngml. Other 24 babies had mean serum prolactin level of 381.06 ng/ml. In group B, out of 25 babies, 15 babies had respiratory distress and required NICU admission having mean prolactin levels of 271.73 ng/ml which was significantly on a lower side. Other 10 babies in the group had mean serum prolactin levels of 304.92 ng/ml. fetal cord mean serum prolactin levels were significantly low in babies who had respiratory distress. Thus babies with RDS had a lower PRL level as compared to babies who did not have RDS.

Discussion

Normally during pregnancy, prolactin (PRL) levels rise gradually from a non-pregnant level of 10-20ng/ml to 180-420 ng/ml at term [1].

But rise is lower if pregnancy is complicated with pregnancy induced hypertension, gestational diabetes mellitus, preterm, intrauterine growth restriction, premature rupture of membrane(PROM), preterm with premature rupture of membranes(PPROM) and anaemia [1, 7].

Following are the important points to be highlighted in our study.

1. The mean cord blood serum prolactin (PRL) levels in Group a (Normal pregnancy) was 376.34 +/- 100.309 ng/ml and in Group B (High risk or abnormal pregnancy) was 285.01 +/- 54.474ng/ml.
2. Cord blood serum prolacin (PRL) levels were directly proportional to gestational age i. e. as the gestational age increases the cord blood serum prolactin (PRL) increases.
3. Prolactin (PRL) levels were very low in high risk pregnancies like Preterm labour, premature rupture of membrane (PROM), Preterm with premature rupture of membranes (PPROM).
4. Cord blood serum prolactin (levels) were low in babies who had RDS than those with non-RDS.
5. Women with complicated / high risk pregnancy had lower serum PRL levels at comparable gestational age as compared to women having normal pregnancies with higher risk of RDS and need for NICU admission.
6. However, limitations of our study is the less number of patients in both the groups. Study of cord blood with more patients is required so that preventive measures can be undertaken depending on the cord blood serum prolactin (PRL) levels.

Conclusion

Along with other hormone parameters like estradiol, cortisol, testosterone, thyroid hormones, glucagon and insulin; prolactin PRL is one of the hormone that plays a role in fetal lung maturation. Cord serum prolactin (PRL) was directly proportional to gestational age in normal and abnormal pregnancies, irrespective of their maternal age, parity, socioeconomic status, geographical background and mode of delivery. Women with abnormal (high risk) pregnancies had significantly lower (285.01 +/- 54.474 vs 376.34 +/- 100.309 ng/ml) prolactin level as compared to that with normal pregnancy. Women with lower PRL levels had higher incidence of babies with RDS as compared to women with higher PRL levels. We conclude from our study that low cord blood serum prolactin levels were strongly associated with adverse neonatal outcome. Estimation of cord blood serum prolactin PRL, in turn can provide a window of opportunity to the clinicians to adopt a preventive treatment.

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