

## **Foetal Cord Serum Prolactin: Levels and Association in Complications of pregnancy and Respiratory Distress Syndrome (RDS)**

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### **Abstract**

The study was carried on 85 newborns to establish a relationship between umbilical cord serum prolactin levels and gestational age, neonatal lung function and maternal complication. Serum cord prolactin level increased from 166.33ng/ml to 379.36ng/ml from 24 to 42 weeks of gestation. A significant association was demonstrated between cord serum prolactin level and birth weight ( $P < 0.001$ ). Newborns that developed RDS had a significant low level of serum prolactin (207.09 ng/ml) as compared to that of non-RDS newborns. The newborns with Apgar score of 7 or less had significantly lower serum prolactin levels than those with Apgar score more than 7 (235.36 ng/ml Vs. 357.05 ng/ml). There was a significant difference between prolactin levels of newborns in normal and abnormal pregnancy (414.61 ng/ml Vs. 312.44ng/ml). Newborns of mothers with PIH had lower prolactin levels as compared to normal (322.67 ng/ml Vs. 414.67 ng/ml). The risk of RDS is less in newborn with high prolactin level than in newborns with low prolactin levels. So prolactin might have a role in fetal lung maturation.

**Keywords:** Fetal cord serum prolactin, Complications in pregnancy, Respiratory distress syndrome

### **1. Introduction**

The role of prolactin in lactation and the factors that serve to regulate pituitary prolactin production in adult humans are reasonably well characterized. On the other hand the determinants of fetal pituitary prolactin production and the role of circulating prolactin that serves in the developing human are less well established.

The progressive rise of prolactin levels during pregnancy is well documented and many studies have been carried out to know the role of prolactin in fetal development. It has been proposed that prolactin may, along with adrenocorticotropin participates in the regulation of adrenal steroid production in human adults and fetuses. It may also play an indirect role in fetal lung maturation by means of inducing adrenal secretion of glucocorticoids. Moreover an augmentation of surfactant lipid synthesis in lung tissue by prolactin has been reported by some but not by all investigators.

Several studies on prolactin in complicated pregnancies have shown correlation between prolactin levels and fetal outcome mainly in terms of development of respiratory distress syndrome. Thus prolactin seems to have a role in lung maturation along with many other factors through a complex mechanism.

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The present study had compared prolactin levels in among the newborns of mothers who had complicated and uncomplicated pregnancy and studied its study various clinical conditions with special reference to respiratory distress syndrome.

#### **1.1 Aims and objectives**

- 1) To study various clinical conditions associated with fetal cord serum prolactin levels among the newborns.
- 2) To compare fetal cord serum prolactin levels among the newborns of mothers who had complicated and uncomplicated pregnancy.
- 3) To study the association of fetal cord serum prolactin levels and various factors among the newborns having Respiratory Distress Syndrome (RDS).

### **2. Materials and methods**

The present study was undertaken from April 2011 to October 2013 at Department of obstetrics and gynecology, Govt. Medical College Akola. The permission from head of the institution and clearance from ethical committee was obtained before starting this study.

A prospective study of randomly selected women delivered in our Hospital, included 24 pregnant women with uncomplicated pregnancy and 56 women with complicated

pregnancy. The pregnancy associated complications included were pregnancy induced hypertension (PIH), premature rupture of membranes (PROM), preterm labor (PTL), intrauterine growth restriction (IUGR), Twins, Gestational diabetes mellitus (GDM).

A detailed history of mothers was taken and a thorough examination was done. The gestational period was calculated from the first day of last menstrual period or by first trimester ultrasound scan or later by re-examination of the newborn. Women with intrauterine death, hypothyroidism and hyperprolactinemia were not included in the study.

The mode of delivery was noted. The newborn was examined for estimation of gestational age, Apgar score at 1 and 5 minutes and for evidence of RDS. The birth weight and sex of the baby was noted.

RDS was determined if baby had:

1. Respiratory rate > 60/minute
2. Diminished air entry in the lungs
3. Presence of chest wall retraction

Babies with RDS were followed in Neonatal Intensive Care Unit (NICU) and observed for development of complications or recovery.

3-5 ml of umbilical cord blood was collected in a plain vial after the delivery of the baby. Sample was sent to lab for prolactin estimation. Examination of prolactin level was done by enzyme immunoassay in vitro diagnostic kit. This method involves a multiple polyclonal antibody enzyme immunoassay mechanism for quantitative determination.

The data was collected after taking informed consent ensuring confidentiality and guarantee of anonymity to the individual. The data was coded, tabulated and analyzed using suitable statistical methods

### 3. Observations & results

The present study involved 85 newborns Out of total 85 newborns studied, 74 had Apgar score (after 1 minute) > 7

and rest 11 had score < 7. They had serum prolactin level 357.05 ng/ml and 253.66 ng/ml respectively. This difference observed was statistically significant (p<0.001).

Majority (71) of newborns enjoyed adequate lactation, but for few (14) babies it was poor. Mean serum prolactin level (353.61 ng/ml and 278.93 ng/ml respectively) was significantly different among these two groups

Out of 85 studied, 11 newborns developed respiratory distress syndrome (RDS) and shifted to NICU and treated accordingly. Serum Prolactin level was significantly associated with the development of RDS as mean serum prolactin level was significantly less for the newborns who developed RDS (207.09 ng/ml) than those who did not (361.26 ng/ml).

Serum Prolactin level went on increasing as birth weight of baby increased and this was statistically significant (p < 0.05).

Similarly prolactin level was also significantly associated with gestational age of newborns. Mean serum prolactin level was significantly higher among the newborns of mothers having complications during the pregnancy (414.67 ng/ml) than those not having it (312.44 ng/ml).

Total 36 newborns were premature. Out of these 11 developed RDS and rest 24 did not. Again out of these 36 premature newborns 13 were put on steroid therapy and 23 were not. Almost 30% newborns in each group developed RDS. Serum Prolactin level was significantly different in these groups also.

Among the complications recorded during pregnancy, PIH was the commonest, observed among 18 cases, followed by PROM (14) and Twins (10). Serum Prolactin level among these groups was 322.67, 356.67 and 277.60 which was significantly less than that observed among the group without any complication.

**Table 1: Distribution of babies according to serum prolactin level and clinical conditions affecting it**

		Number	Mean Serum Prolactin Level (ng/ml)	SD
Apgar Score (After 1 minute)	> 7	74	357.05	77.847
	< 7	11	235.36	57.058
Lactation	Adequate	71	353.61	79.743
	Not Adequate	14	278.93	90.477
RDS in baby	Present	11	207.09	61.473
	Absent	74	361.26	69.378
Complication during Pregnancy	Present	61	312.44	79.381
	Absent	24	414.67	50.517
Birth Wight of Baby (in kg)	0.5- 1	2	198.00	37.00
	1- 1.5	6	211.33	79.76
	1.5-2	17	269.12	42.53
	2-2.5	23	325.52	49.59
	2.5-3	20	404.00	42.161
	3-3.5	9	420.89	40.60
	> 3.5	8	413.38	62.11
Gestational Age	28-31	3	166.33	66.16
	31-34	7	213.71	76.56
	34-37	26	309.26	77.88
	37-42	49	379.37	63.03

**Table 2: Distribution of babies according to serum prolactin level and Respiratory Distress Syndrome (RDS)**

		Number	%	Mean Serum Prolactin Level (ng/ml)	SD
Preterm Delivery	RDS Present	11	30.55	207.09	61.47
	RDS Absent	25	69.44	327.08	62.25
Babies with Steroid therapy	RDS Present	4	30.76	204.00	26.012
	RDS Absent	9	69.23	281.67	39.395
Babies without Steroid therapy	RDS Present	7	30.43	208.85	77.14
	RDS Absent	16	69.56	348.19	57.80

**Table 3: Prolactin levels in Uncomplicated and Complicated pregnancy**

Pregnancy Complication	Number	Mean Serum Prolactin Level (ng/ml)	SD
Normal	24	414.67	50.517
PIH	18	322.67	105.59
PROM	14	356.57	77.64
Preterm	8	297.12	100.90
IUGR	6	369.83	71.16
Twins	10	277.60	57.94
GDM	5	294.40	103.90
Total Preterm delivery	36*	288.44	80.44

\*includes babies delivered before 37 weeks of pregnancy

#### 4. Discussion

Prolactin is single chain polypeptide of 199 amino acids with a molecular weight of 23,000 Daltons, 40% similar in structure to growth hormone and placental lactogen.

Prolactin gene expression occurs in the anterior pituitary gland, in decidualized endometrium and myometrium. Prolactin secreted in these various sites is identical.[1]

Pituitary secretion of prolactin is chiefly under inhibitory control of hypothalamic dopamine released into the portal circulation, a tonic inhibition that requires a high output of dopamine.[1]

Prolactin homeostasis is regulated mainly by prolactin itself, feeding back on the dopamine releasing neurons.

During pregnancy, prolactin levels rise from normal level of 10-25 ng/ml, to high concentration, beginning about 8 weeks and reaching a peak of 200-400ng/ml at term.[1]

In our study with 80 pregnant women (24 with normal pregnancy and 56 with complicated pregnancy) and their 85 newborns, we observed that mean cord serum prolactin levels increased with gestational age in both normal and abnormal pregnancy. A highly significant variation as a function of gestational age was noted similar in many previous studies.[2,3]

In normal pregnancy mean cord serum prolactin level increased from 364 ± 41 ng/ml at 34-37 weeks to 420.5 ± 48.08 ng/ml at 37-42 weeks. In abnormal pregnancy group, mean prolactin level increased from 166.36 ± 66.16 ng/ml at 28-31 weeks to 345.85 ± 63 ng/ml.

But the rise in prolactin level was lower in pregnancy with complications as observed in previous two studies .[2,3]The mean cord serum prolactin level in abnormal pregnancy, 312.44 ± 79.38 ng/ml was much lower than the level observed in normal pregnancy i.e. 414.67 ± 50.51ng/ml.

We observed a positive correlation of cord serum prolactin levels with increasing birth weight of the newborns. Similar to the findings of previous studies.[2,3] The levels increased from 198 ± 35 ng/ml in 0.5 - 1 kg group to 420.89 ± 62.11 in 3 - 3.5 kg group.

There was no significant difference in mean cord serum prolactin levels in relation to socio-economic status of the mother and age of the mother as observed in studies done by Dayal Malhotra *et al* [1] and Jindal Promila *et al*.[3]

There was no significant difference in mean levels of cord serum prolactin in relation to mode of delivery of the newborn as observed in previous studies. [2,3]

Mean cord serum prolactin levels did not differ significantly in male and female newborns.[2]

In present study, the mean cord serum prolactin levels were significantly lower in infants with RDS as compared to healthy newborns, raising the possibility of role of prolactin in lung maturation (207.09 ± 61.47 ng/ml Vs 361.26 ± 69.37ng/ml). Our observation correlates with findings of previous studies by many investigators.[2]

Out of 36 babies, who delivered before 37 completed weeks of gestation 11 babies (30.55%) developed RDS and had mean prolactin levels 207.09 ± 61.47 ng/ml, which are significantly lower than the mean prolactin levels of 25 babies (69.44%) without RDS, i.e. 327.09 ± 62.25 ng/ml. This group includes babies of mothers who came into preterm labor and those pregnancies which required termination before 37 weeks because of pregnancy complications.

Out of 36 preterm deliveries, 13 babies (36.11%) received betamethasone prophylaxis 24 hours before delivery. 4 out of 13 babies (30.76%) developed RDS and had mean cord serum prolactin level of 204 ± 26.01 ng/ml.

9 out of 13 babies (69.23%) did not develop RDS and had higher mean prolactin levels i.e. 281.67 ± 39.39 ng/ml.

Out of 36 preterm deliveries, 23 babies (63.88%) did not receive betamethasone prophylaxis. 7 babies (30.43%) in this group developed RDS and had mean cord serum prolactin level of  $208.85 \pm 77.14$  ng/ml, which is lower than prolactin levels of babies without RDS i.e.  $348.19 \pm 57.80$  ng/ml.

Percentage of babies with RDS in steroid and non-steroid group was almost same and there was no significant difference prolactin level in these two groups. Administration of betamethasone did not affect the incidence of RDS and prolactin levels in preterm newborns. Our observation correlates with that done by other investigators.[4] It was contradictory to observations done by Gluckman *et al* [4] and Jindal Promila *et al.*[3] They observed decreased incidence of RDS and increased prolactin levels in preterm babies which received betamethasone prophylaxis.

We observed significant difference in mean cord serum prolactin levels in babies with apgar at one minute  $< 7$  and  $> 7$ . Babies with apgar  $< 7$  had lower prolactin levels than babies with apgar  $> 7$  ( $235.36 \pm 37.05$  ng/ml Vs  $357.05 \pm 77.84$  ng/ml). Our observation correlates with that of Dayal Malhotra *et al*[2].

The mean prolactin levels in babies of mother with PIH were lower than babies of normal pregnant woman ( $322.67 \pm 105.59$  ng/ml Vs  $414.67 \pm 50.51$  ng/ml). This finding was similar with those of Jindal Promila *et al.*[3]

3 babies in PIH group developed RDS and had mean prolactin level  $201.37 \pm 44$  ng/ml. All the 3 babies were delivered prematurely, out of these 2 babies died.

The mean cord serum prolactin level in diabetic pregnancy was lower;  $294.40 \pm 103.90$  ng/ml as compared to normal pregnancy i.e.  $414.67 \pm 50.51$  ng/ml. One baby (20%) out of 5 babies with GDM developed RDS which was delivered at 36 weeks.

In our study, all babies who developed RDS were delivered prematurely and had risk factors like PIH, PROM, Preterm labor, GDM and twins. They had lower mean cord serum prolactin level than non-RDS babies ( $288.44 \pm 80.44$  Vs  $361.26 \pm 69.37$  ng/ml).

Babies delivered to mothers with PROM had lower prolactin levels ( $356.57 \pm 77.64$  ng/ml Vs  $414.67 \pm 50.51$  ng/ml) and our findings correlates with those observed by Jindal Promila *et al.*[3]

The mean cord serum prolactin level for twin pregnancy was  $277.60 \pm 57.94$  ng/ml Vs  $414.67 \pm 50.51$  ng/ml). Out of 10 twins involved in this study, 1 twin developed RDS and had even lower prolactin level i.e. 175 ng/ml. Our finding in babies with twins, correlates with Jindal Promila *et al.*[3]

Babies of mothers with IUGR had lower mean prolactin levels than normal pregnancy ( $369.83 \pm 71.16$  ng/ml Vs  $414.67 \pm 50.51$  ng/ml). But mean prolactin level in IUGR babies was more than mean prolactin levels for abnormal pregnancy ( $369.83 \pm 71.16$  ng/ml Vs  $312.44 \pm 79.38$  ng/ml). All IUGR pregnancies had oligohydramnios. Our finding is contradictory to that of previous study.[3]

Mean cord serum prolactin levels were more in mothers with adequate lactation than with mothers who were not lactating adequately ( $353.61 \pm 79.74$  ng/ml Vs  $278.93 \pm 90.47$  ng/ml). Our finding correlates with that of previous study.[3]

## 5. Conclusion

On the basis of this study, it is clear that there is marked increase in prolactin levels with increase in gestational age and prolactin levels are lower in babies with RDS than in babies without RDS of comparable gestational age. Prolactin levels are lower in pregnancies with complications.

In view of lower prolactin levels in RDS and positive association with gestational age, it might be suggested that prolactin has a role in fetal lung maturation.

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