

A Comparison of Fetal Cord Serum Prolactin Levels in Normal and High Risk Pregnancies

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ABSTRACT

Objective: To compare the cord blood serum prolactin levels of normal and high risk pregnancies.

Method: Cord blood prolactin levels of 40 newborns of normal pregnancy and 40 newborns of high risk pregnancies were compared. Follow up of newborns done for development of respiratory distress. Results were statistically analyzed.

Result: Mean prolactin of cases was 318.24 ± 33.25 ng/ml and of controls was 410.98 ± 33.13 ng/ml. 100 % of newborn with prolactin ≤ 300 ng/ml developed respiratory distress while only 17.4% newborn with prolactin 301-350 ng/ml had respiratory distress. Mean prolactin of healthy newborns was 382 ± 47.55 ng/ml and of distressed newborns was 307.22 ± 47.10 ng/ml.

Conclusion: It is concluded from study that low cord blood serum prolactin levels are strongly associated with adverse neonatal outcome and level can be used as a screening test of at risk newborn thus allowing clinician to intervene with a potential preventive treatment.

KEYWORDS: Newborn, Prolactin, Respiratory distress.

INTRODUCTION

Prolactin, also called luteotropic hormone is a peptide hormone discovered by Henry Friesen¹. It is encoded by PRL gene on chromosome 6 and molecular weight of about 23kDa contains 199 amino acid residues and 3 disulfide bridges and has considerable structural similarity to human growth hormone.²

More than 300 separate actions of prolactin are reported including effects on water and salt balance, growth and development, metabolism, brain and behaviour, reproduction and immune regulation.³ Several hormones (estradiol, cortisol, testosterone, thyroid, glucagons, insulin) have been implicated in surfactant biosynthesis in lungs of foetus. Prolactin is the latest hormone to be added to the list of hormones affecting lung maturation but this is still not well established.⁴

This study was undertaken to establish the role of prolactin in lung maturation and hence in development of respiratory distress.

MATERIALS AND METHODS

This descriptive comparative study was conducted in the Department of Obstetrics and Gynaecology, SMS

Medical College, Jaipur during the year 2012-2013. Total no. of women (n=80) were subjected to detailed history taking, general physical examination, obstetric examination and routine antenatal investigation i.e. blood grouping, CBC, urine albumin/sugar, random blood sugar, HBsAg, VDRL, HIV screening and ultrasound scan. Gestational age was calculated from the first day of last menstrual period.

Exclusion criteria were included in patients with gestational age <37 weeks, LMP not known, multifetal pregnancies, congenital anomaly and intrauterine death of foetus, known case of hypothyroidism and hyperprolactinemia presence of meconium and birth asphyxia.

After screening, the patients were divided into two groups: cases and controls (40 patients in each group):

Group A (Cases): High risk pregnancies, like pregnancy-induced hypertension, gestational diabetes mellitus, premature rupture of membranes, polyhydramnios, oligohydramnios, and anemia.

Group B (Controls): Normal pregnancies.

Mode of delivery was noted. After delivery, 3 mL of mixed umbilical arterial and venous blood was collected in a plain vial. Prolactin estimation of the serum was done by Prolactin Enzyme Immunoassay.

Neonatologist resuscitated the newborn. Following parameters were noted:

1. Apgar score at 1 and 5 minutes
2. Birth weight
3. Gestational age
4. Any signs of respiratory distress

Statistical tests as appropriate were used to compare parameters between the groups.

RESULTS

The present study showed that 82.5% of cases had prolactin ≤ 350ng/ml while 97.5% of controls had prolactin ≥ 350 ng/ml. Mean prolactin of cases was 318.24 ± 33.25 ng/ml and of controls was 410.98 ± 33.13ng/ml. (p<0.05) (Table 1)

Mean prolactin levels in controls at 37,38, 39 and 40 weeks of gestation were 375.77 ± 23.93, 404.43 ± 10.52, 443.25 ± 17.41 and 451.7 ± 11.4 ng/ ml and in cases

mean prolactin levels at same gestational age were 284.6 ± 19, 317.49 ±11.81, 335.22 ± 29.09 and 371.1 ± 22.06 ng/ml. (r>.01) (Table 2) Controls with prolactin levels with 320.45, 379.03 ±13.46, 416.86 ±14.21 and 459.37±6.37 ng/ml had birth weight 2.4, 2.6 ± 0.10,2.84±.08 and 3.13 ± 0.10kg respectively. Cases with prolactin levels 275.12±13.45, 324.42 ± 13.23, 364.65 ± 9.21and 402.25 ng/ml had birth weight 2.59 ± 0.15, 2.84 ± 0.14, 3.05 ±.09 and 3.2 kg respectively. (r >0.01) (Table 3)

Mean cord blood prolactin levels in pregnancies affected with premature rupture of membranes, pregnancy induced hypertension, oligohydramnios, gestational diabetes mellitus, anemia and polyhydramnios were 296.19 ± 21.50, 300.87 ± 28.48, 329.93±32.66, 330.68 ±14.65, 334.92±29.89 and 356.32±29.26ng/ml respectively. (p<0.05) (Table 4) 100 % of newborn with prolactin ≤ 300 ng/ml developed respiratory distress while only17.4% newborn with prolactin 301-350 ng/ml had respiratory distress. Mean prolactin of healthy newborns was 382 ± 47.55 ng/ ml and of distressed newborns was 307.22 ± 47.10 ng/ml. (P< 0.05) (Table 5)

Table 1: Prolactin levels in cases (Group A) and controls (Group B)

S.No.	Prolactin (ng/ml)	Case (Group A)		Control(Group B)	
		No.	Percentage %	No.	Percentage %
1	≤300	11	27.5%	-	-
2	301-350	22	55%	1	2.5%
3	351-400	6	15%	11	27.5%
4	401-450	1	2.5%	21	52.5%
5	>451	-	-	7	17.5%
	Total	40		40	
	Mean Prolactin		318.24 ± 33.25		410.98 ± 33.13

Table 2: Correlation of prolactin level with gestational age

S. No.	Prolactin (ng/ml)	Gestational age (Weeks)												
		37W			38W			39W			40W			
		Ca	Cont	T	Ca	Cont	T	Ca	Cont	T	Ca	Cont	T	
1	≤300	9 (81.8%)	-	9	1 (6.7%)	-	1	1 (10%)	1	1	-	-	-	
2	301-350	2 (18.2%)	1 (9%)	3	14 (93.3%)	-	14	5 (50%)	5	1 (25%)	-	1	1	
3	351-400	-	8 (72.8%)	8	-	3 (20%)	3	4 (40%)	4	2 (50%)	-	2	2	
4	401-450	-	2 (18.2%)	2	-	12 (80%)	12	-	5 (50%)	5	1 (25%)	2 (50%)	3	
5	≥451	-	-	-	-	-	-	-	5 (50%)	5	-	2 (50%)	2	
	Total			22			Total		30	Total		20	Total	8

Ca: Case, Cont: Control, T: Total

Table 3: Correlation of birth weight with prolactin level

S No.	Birth weight	Prolactin Level (ng/ml)									
		≤300		301-350		351-400		401-450		≥451	
		Ca	Cont	Ca	Cont	Ca	Cont	Ca	Cont	Ca	Cont
1	≤2.5	5 (45.5%)	-	-	1 (100%)	-	4 (36.4%)	-	-	-	-
2	2.51-2.80	5 (45.5%)	-	10 (45.5%)	-	-	7 (63.3%)	-	8 (38.1%)	-	-
3	2.81-3.10	1 (9%)	-	10 (45.5%)	-	4 (66.7%)	-	-	13 (61.9%)	-	2 (28.6%)
4	≥3.11	-	-	2 (9%)	-	2 (33.3%)	-	1 (100%)	-	-	5 (71.4%)
Total		11	-	22	1	6	11	1	22	-	7
MeanBW		2.59 ±0.15	-	2.84 ±0.14	2.4	3.05 ±0.09	2.64 ±0.1	3.2	2.84 ±0.08	-	3.13 ±0.1
Prolactin		275.12± 13.45	-	324.42 ±13.23	320.45	364.65± 9.21	379.03± 13.46	402.25	416.86± 14.21	-	459.37± 6.37

Ca: Case, Cont: Control, T: Total

Table 4: Correlation of prolactin level with risk factor

S. No.	Prolactin level (ng/ml)	Risk factor					
		PIH	PROM	OLIGO	GDM	Anemia	POLY
1	≤300 (275.01)	7(53.8%)	3(60%)	1(12.5%)	-	-	-
2	301-350 (324.42)	5(38.5%)	2(40%)	5(62.5%)	2(66.7%)	5(71.4%)	2(50%)
3	351-400 (364.65)	1(7.7%)	-	2(25%)	1(33.3%)	1(14.3%)	1(25%)
4	401-450 (402.25)	-	-	-	-	1(14.3%)	1(25%)
Total		13	5	8	3	7	4
Mean prolactin (ng/ml)		300.87± 28.48	296.19± 21.50	329.93± 32.66	330.68± 14.65	334.92± 29.89	356.32± 29.26

Table 5: Correlation of prolactin level with respiratory distress

S. No.	Prolactin (ng/ml)	Respiratory distress					
		Group A (case)			Group B (control)		
		Yes	NICU Adm	No	Yes	NICU Adm	No
1	≤300	11	11	11	-	-	-
2	301-350	23	4	2	18	1	1
3	351-400	17	-	-	6	2	-
4	401-450	22	-	-	1	-	-
5	≥451	7	-	-	-	-	-
Total		80					

DISCUSSION

This study compared the cord blood serum prolactin level of normal and high risk pregnancies and correlation of cord blood serum prolactin levels with development of respiratory distress in newborn was evaluated. Higher prolactin levels in study were contributed from the controls. None of the control had prolactin level ≤ 300ng/ml. None of the case had prolactin level ≥ 451ng/ml. Similar results were studied by Jindal Promila, Singh Daljit, Goyal Anupama⁵ in 2005.

High risk pregnancies had significantly lower prolactin levels (302.12± 103.02 v/s 385.65 ± 85.01ng/ml) as compared to normal pregnancies. Positive correlation of prolactin level with gestational age and birth weight was found. Prolactin levels both in cases and controls increased with gestational age and birth weight. But prolactin levels were much lower in case compared to controls at same gestational age and birth weight. Mean prolactin level in controls at 37 weeks of gestational age

was 375.77 ± 23.93 ng/ml which increased to 404.43 ± 10.52 ng/ml at 38 weeks. Mean prolactin level in cases at 37 weeks of gestation was 284.6 ± 19 ng/ml which increased to 317.49 ± 11.81 ng/ml at 38 weeks. In controls mean prolactin level at 39 weeks of gestational age was 443.25 ± 17.41 ng/ml, which increased to 451.7 ± 11.4 ng/ml at 40 weeks. While in cases mean prolactin level at 39 weeks of gestation was 335.22 ± 29.09 ng/ml which increased to 371.1 ± 22.06 ng/ml at 40 weeks of gestation. Hercz P. Acta Med Hung et al⁶. in 1985 also found an increase in the prolactin level from 28th to 40th week of gestation. 91% of cases who had prolactin ≤ 300 ng/ml, had birth weight ≤ 2.8 kg.

Mean birth weight in cases at prolactin ≤ 300 ng/ml was 2.59 ± 0.15 kg. None of the cases with >300 ng/ml had birth weight <2.5 kg. Mean birth weight was 2.84 ± 0.14 kg with prolactin level in the range of 301-350 ng/ml. Two newborn in this range although had birth weight more than mean i. e. > 2.84 but they had lower prolactin level as expected with their birth weight. Both of them had diabetic (GDM) mother and their prolactin level were 330.85 and 348.55 ng/ml and their birth weight were 3.25, 3.2 kg respectively. At prolactin level of 351-400 ng/ml mean birth weight 3.05 ± 0.09 ng/ml.

Among 40 controls, 39 had had prolactin level >350 ng/ml, only one had level of 320.45 ng/ml. Mean birth weight in controls with prolactin in the range 351-400 ng/ml was 2.6 ± 0.10 kg. 36% of these had weight ≤ 2.5 kg and 64 % had weight > 2.5 kg. At the range of 401-450 ng/ml mean birth weight was 2.84 ± 0.08 kg. 62% had weight > 2.8 kg and 38 % had weight < 2.8 kg. At prolactin ≥ 450 ng/ml mean birth weight was 3.13 ± 0.10 kg. Among these newborns 29 % had weight <3.1 kg and 71 % had weight ≥ 3.1 kg. Parker CR Jr et al⁷ in 1989 also found same results. In their study serum prolactin levels rose between 24 and 42 weeks' gestation, correlating significantly ($p < 0.01$) with birth weight ($r = 0.32$). Among infants of similar weight those delivered to high risk pregnancies had lower prolactin levels compared to normal pregnancies.

Premature rupture of membrane most severely affects prolactin level (mean prolactin 296.19 ± 21.50 ng/ml). Newborns of mothers who had pregnancy induced hypertension also had low prolactin level. Mean prolactin level of these cases was 300.87 ± 28.48 ng/ml. Mean prolactin level of newborn was 329.93 ± 32.66 ng/ml in pregnancies with oligohydramnios. Mean prolactin level of newborn delivered to diabetic mother was 330.68 ± 14.65 ng/ml. Risk factors like anemia polyhydramnios had not much effect on prolactin level of newborn, mean prolactin level of these cases was 334.92 ± 29.89 ng/ml and 356.32 ± 29.26 ng/ml. Dayal M, Malhotra K, Mukherjee K et al in 2001⁸ also found that newborn of high risk pregnancy had significantly lower (310.37 ± 32.94 ng/ml v/s 395.98 ± 33.95 ng/ml) prolactin

level as compared to that with normal pregnancy, which was in accordance to the present study.

All of the 11 newborns having prolactin level ≤ 300 ng/ml, developed respiratory distress. All of these admitted to NICU. 5 of these babies were of PIH mothers, 3 from each of oligohydramnios, PROM and GDM. Out of these 11 newborn 2 newborn had very low prolactin level of 270.95 and 290.35 ng/ml. They had severe respiratory distress. Their APGAR score at 5 min were 5, remain admitted to NICU for 5 days but after all resuscitative measures they could not be revived and expired on 6th day. One control also developed severe respiratory distress with APGAR score of 5 at birth and 6 at 5 min was admitted to NICU. Baby was of 37 weeks and birth weight was 2.4 kg and prolactin level was 320.45 ng/ml. García León JF, Garza Fernández L, et al⁹ in 1995 analyzed of the predictive value of prolactin concentration in the umbilical cord as an evaluation parameter for respiratory insufficiency in the newborn. The risk for respiratory distress was higher in newborns whose prolactin level was low (10th percentile) than in infants whose prolactin level was high (90th percentile). These results suggested that prolactin had important role in foetal lung maturation.

CONCLUSION

We concluded from our study that low cord blood serum prolactin levels are strongly associated with adverse neonatal outcome. Routine estimation of cord blood prolactin level at birth may help in selecting cases in which strict neonatal monitoring may be required. Thus, cord blood prolactin level can be used as a screening test of at risk newborn thus allowing clinician to intervene with a potential preventive treatment. However larger studies are required to establish cord blood serum prolactin level as a marker of neonatal outcome.

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