J Obstet Gynecol India Vol. 55, No. 5 : September/October 2005 Pg 419-423

ORIGINAL ARTICLE

The Journal of Obstetrics and Gynecology of India

Fetal cord serum prolactin level in normal and abnormal pregnancies

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OBJECTIVE(S): To study the role of prolactin in the development of respiratory distress syndrome (RDS) in newborns.

METHOD(S): In this prospective study of 100 women, 20 with normal pregnancy and 80 with abnormal pregnancies (pregnancy-induced hypertension, gestational diabetes mellitus, premature labor, premature rupture of membranes, twins, jaundice and anemia), umbilical cord blood was taken at the time of delivery for serum prolactin (PRL) level estimation and newborns were observed for development of RDS.

RESULTS: Cord serum PRL level was directly proportional to gestational age and birth weight in normal and abnormal pregnancies but was not affected by maternal age, parity, socioeconomic status, geographical background and mode of delivery. Women with abnormal pregnancy had significantly lower (302.12± 103.02 vs 385.65 ± 85.01 ng/mL) prolaction level as compared to that with normal pregnancy. Newborns who developed RDS had significantly lower (147.92 vs 329.72 ng/mL) cord serum prolactin level. Out of 15 babies exposed to betamethasone in-utero 80% had higher prolactin level (279.66 ±138.30 vs 166.96 ± 14.43 ng/mL) and did not develop RDS as compared to babies who developed RDS (P = 0.013).

CONCLUSION(S) : Prolactin does play a role in fetal lung maturation.

Key words : respiratory distress syndrome, cord serum prolactin level, lung maturation.

Introduction

Hyaline membrane disease (HMD) is the most common cause of respiratory distress syndrome (RDS) leading to mortality / morbidity in preterm babies. Adequacy of lung surfactant ensures alveolar stability that is required to establish effective ventilation at the time of first breath. Several hormones (estradiol, cortisol, testosterone, thyroid hormones, glucagons, insulin) have been implicated in the production of lung surfactant. Prolactin in increasing concentration through a complex mechanism seems to participate in pulmonary maturation [1], but this is still not well established. This study was undertaken to establish the role of prolactin in lung maturation and hence in development of RDS.

Methods

This study included 100 randomly selected pregnant women admitted to labor room. Twenty women with normal pregnancies constituted Group A and 80 with complications of pregnancy like pregnancy-induced hypertension (PIH), gestational diabetes mellitus (GDM), premature labor, premature ruptue of membranes (PROM), intrauterine growth retardation (IUGR), twins, jaundice and anemia constituted Group B. In every woman, detailed history was taken and examination with special reference to medical problems, PIH, GDM etc. was carried out. Gestational age was calculated from the first day of last menstrual period (LMP) if the woman was sure of dates; if not, then from either sonography done in the 1st trimester or from the date of quickening. Those with hyperprolactinemia, hypothyroidism, and intrauterine death were excluded from the study. Mode of delivery was noted. Neonatologist who had no knowledge of the study resuscitated the newborn. Apgar score at l and 5 minutes, birth weight and gestational age were noted. The baby was said to have RDS, if respiratory rate was > 60/minute, air entry in the lungs was diminished or presence of subcostal and intercostal recession was present.

Without squeezing the cord, 3 mL of mixed umbilical arterial

Paper received on 09/06/2005 ; accepted on 09/07/2005

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and venous blood was collected in a plain vial just after delivery of the newborn. Sample was kept at room temperature. The serum was separated from the cord blood sample. Prolactin estimation was done by Lee Bead Prolactin Enzyme Immunoassay. This employs a multiple polyclonal antibody enzyme immunoassay mechanism for quantitative determination of human PRL hormone in serum. Mothers were observed for the adequacy of lactation.

Results

The women in the two groups were comparable in age, parity, socio-economic status, and geographical background. Cord serum prolactin levels were found to have no correlation with any of these factors.

In both normal and abnormal pregnancies, mean cord serum prolactin levels increased with increase in gestational age. In Group A, with increase in gestation from 34-37 weeks to 37-42 weeks, prolactin levels increased from 330.85 ± 68.11 to 410.83 ± 90.65 ng/mL. In Group B, levels increased from 89.32± 93.96 ng/mL to 397.61± 115.53 ng/mL with increase in gestational age from 22-28 weeks to 34-37 weeks and decreased (364.22 ± 96.67 ng/mL) at term i.e 37-42 weeks (Table 2). The difference between the 37-42 weeks levels in the two groups was statistically significant (P = 0.04). Women with complicated pregnancies (Table 1) achieved significantly lower levels (302.122 ± 103.02 vs 385.64± 85.01 ng/mL, P = 0.015) as compared to women without any complications.

Prolactin levels were directly proportional to the birth weight in both the groups. In Group B, with birth weight of < 500 g the mean level was 19.38 ± 8.05 ng/mL (Table 3) whereas with 3001-3500 g birth weight the level was 376.34 ± 103.85 ng/mL which is significantly lower (P = 0.032) than 413.63 ± 97.86 ug/mL with 3001-3500 gm birth weight in normal pregnancy. Even babies weighing more than 3500 g had significantly lower (P = 0.011) prolactin level in Group B than in Group A (335.7± 189.92 ng/mL vs 470 ng/mL).

Out of the 106 babies born, 12 (11.32%) developed RDS, their mothers delivered prematurely (Table 1, 2 and 4) and had pregnancy related complications (16.66% GDM, 25% PIH, 16.66% PROM). 41.66% of RDS babies were twins. None of the babies in normal pregnancy developed RDS.

Prolactin level of RDS babies ranged between 22 and 210.7 ng/mL (Figure 1). The mean was 147.92 ± 61.80 ng/mL which was significantly lower (P < 0.01) in comparison with that of non-RDS babies (Table 4).83.33% (10/12) RDS babies (Figure 1) had prolactin levels less than 211 ng/mL.

Fifty-nine women (66 babies) with normal and abnormal pregnancy were admitted with premature labor or required to be delivered prematurely (Table 2). Only 13 women (15 babies) received betamethasone for lung maturation (Table 5). Of these 15 babies, 12 had higher prolactin levels (279.66 ± 138.30 ng/mL) and did not develop RDS whereas three who developed RDS had significantly lower prolactin values

Table 1. Correlation of cord serum prolactin level with normal and abnormal pregnancies and RDS babies.

	No.	%	Prolatin level Mean±SD (ng/mL)	No. (%) of RDS babies
Women with normal pregnancy	20	100.0	385.64 ± 85.01	
Women with abnormal pregnancy	80 [c]	100.00	302.122 ± 103.02[a]	
• Pregnancy induced hypertention	22	20.56	348.06 ± 137.12	3 (25.00) [b]
• Gestational diabetes mellitus	6	5.6	326.53 ± 157.80	2 (16.66) [b]
• Premature rupture of membrances	8	7.47	33.37 ± 84.08	2 (16.66) [b]
• Premature labor	38 [c]	35.5	333.65 ± 138.61	12 (100.00) [b]
• Twins	6 [c]	5.6	215.02 ± 148.73	5 (41.66) [b]
• Jaundice	5	4.67	329.04 ± 74.93	
• Intrauterine growth retadation	10	9.34	407.85 ± 132.19	
• Anemia	9	9.4	365.8 ± 119.97	
• Polyhydramnios	3 [c]	2.8	397.4 ± 63.50	
Total				12(100.00) [b]

[a] P = 0.015

[b] Babies born to women with multiple complications

[c] Number of women having multiple complications.

Table 2. Correlation of cord serum prolactin levels and RDS with gestational age.

Gestational age (weeks)	GROUP A						GROUP B					
	Number of women	Mean cord serum PRL (ng/mL) (mean±SD)	Babies with RDS		Babies without RDS		No. of women	Mean cord serum PRL (ng/mL) (mean±SD)	Baies with RDS		Babies without RDS	
			Number	Percent	Number	Percent			Number	Percent	Number	Percent
22-28	-	-	-	-	-	-	8 [c]	89.32 ± 93.56	4	33.33	4	5.40
> 28.31	-	-	-	-	-	-	4 [c]	154.6 ± 71.48	1	8.33	3	4.05
> 31-34	-	-	-	-	-	-	29 [c]	276.2 ± 128.10	5	41.66	24	32.43
> 34-37	4	330.85±68.11[a]	-	-	4	20.00	21	397.61 ± 115.53[a]	2	16.66	19	25.67
> 37-42	16	410.83 ±90.65[b]	-	-	16	80.00	24	364.22 ± 96.67[b]	-	-	24	32.43
Total	20		-	-	-	-	86		12	100.00	74	100.00

[a] P = 0.98 (Non-significant) [b] P = 0.04 (Significant) [c] Includes women with twin gestation.

Table 3. Correlation of cord serum prolactin levels with birth weight.

Birth Weight (g)	Group A (n=20)		Group B (n=80)		P value
	Number	ng/mL (Mean ±SD)	Number	ng/mL (Mean ±SD)	
<500	-	-	3	19.38 ± 8.05	-
501-1000	-	-	6	207.02 ± 208.16	-
1001-1500	-	-	7	208.37 ± 133.20	-
1501-2000	-	-	29	298.34 ± 127.61	-
2001-2500	-	-	10	332.51 ± 126.4	-
2501-3000	7	302.84 ± 65.04	16	350.6 ± 100.47	1.01 (NS)
3001-3500	11	413.63 ± 97.86	13	376.34 ± 103.85	0.032 (S)
>3500	2	470 in both	2	335.7 ± 189.92	0.011 (S)

S = Statistically Significant NS = Non-signifiant

Table 4. Cord serum prolactin levels in RDS and non-RDS Babies.

Babies	Group A			Group B			P value
	No.	%	ng/mL (Mean ±SD)	No.	%	ng/mL (Mean ±SD)	
With RDS	0	0	-	12	13.95	147.92 ± 61.80	
Without RDS	20	101	385.65 ± 85.01	75	86.05	329.70 ± 129.9	0.82 (NS)
Total	20	100		86	100		

RDS = Respiratory distress syndrome NS = Non-significant

Table 5. RDS babies and in-utero exposure to betamethasone.

	RDS			No RDS			P value
	Number	Percent	Prolactin level (Mean±SD)	Number	Percent	Prolactin level (Mean±SD)	
Betamethasone group (n=15)	3	20.00	166.96 ± 14.42[a]	12	80.00	279.66 ± 138.30[a]	0.013[a] (Significant)
Non-betamethasone group (n= 91)	9	9.9	114.47 ± 81.05[b]	82	90.10	361.84 ± 102.80[b]	0.028[b] (Significant)

RDS - Respiratory distress syndrome

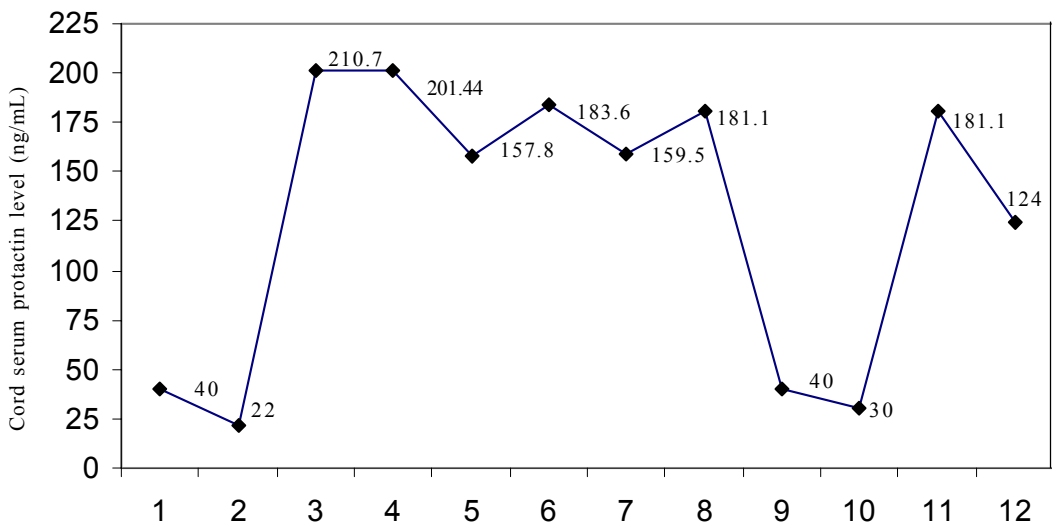

Figure 1. Cord serum prolactin levels of the 12 RDS babies

(166.96 ± 14.43) ng/mL) (P 0.013). In women who did not have betametbasone, nine babies developed RDS and had significantly lower (P=0.28) mean prolactin levels (114.47 ± 81.05 ng/mL vs 361.84 ± 102.80 ng/mL) than those babies who did not have RDS.

Cord serum prolactin levels had no correlation with the mode of delivery. In all, 58.49% (62/106) babies were born vaginally, and of these 12.90% (8/62) developed RDS. Out of the total 12 RDS babies, five survived. Eighty-six percent (86/100) of women lactated adequately and had higher prolactin levels (Group A – 385.64 ± 85.01 ng/mL; Group B – 345.41± 112.19 ng/mL), whereas women with inadequate lactation had lower values (Group A – No woman; Group B – 108.9 ± 63.55 ng/mL).

Discussion

Prolactin, apart from its other actions, is thought to play some role in lung surfactant development. Even normally also during pregnancy, prolactin levels increase gradually from non-pregnant levels of 10-20 ng/mL to 200-400 ng/mL at term [2]. But this rise is lower if the woman develops some pregnancy related complication [2]. In our study too, mean cord serum prolactin levels were directly proportional to gestational age in both normal and abnormal pregnancies and the levels were significantly lower (302.12±103.22 v/s 385.64 ± 85.01 ng/mL) in women with PIH, PROM, GDM and IUGR.

Diabetes mellitus, per se, is believed to delay lung maturation and offsprings of diabetic mothers are significantly affected by RDS [3]. Cord serum prolactin levels were found to be low in new borns of diabetic mothers. We too, had the same findings. Mean cord serum prolactin levels of women with GDM were lower as compared to those of women with normal gestation (326.53 ± 157.80 vs 385.64 ± 85.01 ng/mL; P=0.015).

Prematurity is the most important cause of RDS. All our RDS babies were premature and their mothers had one or more problems (PIH, GDM, PROM etc) during antenatal period. Besides prematurity, these babies had significantly lower prolactin level (147.92±61.80 ng/mL) than non-RDS babies (329.70 ± 129.9 ng/mL). This is consistent with many other reports [1,2,4].

In our study, mode of delivery had no effect on cord serum prolactin levels. They were found to be directly proportional to birth weight in both normal and abnormal gestations. Leurti et al [5] also report the same.

In-utero betamethasone therapy enhances lung maturation [6] and if given at least 72 hours before delivery, it gives protection against RDS [7]. But still serum cord prolactin level can be the determining factor for the development of RDS. In our study, among babies exposed to betamethasone antenatally, only 20% developed RDS, and those had lower mean prolactin level (166.96 ± 14.42 ug/mL) whereas 80% with higher level of 279.66 ± 138.30 ng/mL did not develop RDS (P=0.013). We had a chance to compare the effect of birth weight, gestational age and apgar score on RDS in a case of twins delivered by LSCS at 33 weeks of gestation. Both babies had almost the same birth weight (1.74 kg and 1.76 kg) and same apgar score (5 at 1 and 8 at 5 minutes) but the baby with lower cord serum prolactin level (181.1 ng/mL) developed RDS whereas the baby with higher serum prolactin level (253 ng/mL) did not develop it. This strengthens the view that prolactin plays an important role in lung maturation.

In the postpartum period, women with higher mean prolactin level (Group A 385.64 ± 85.01 ng/mL; Group B 345.41 ± 112.19 ng/mL) lactated adequately, whereas, women who had insufficient lactation had lower prolactin levels (Group A- no woman; Group B 108.09 ± 63,55 ng/mL). Thus, the risk of RDS is considerably less in the newborns with higher serum prolactin levels than in the newborns with lower serum prolactin levels, whereas gestational age and birth weight have indirect relationship with RDS development. Lung maturation is also governed by prolactin level.

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