

## Evaluation of Cord Blood Serum and Maternal Serum Cortisol in Fetal Distress

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**OBJECTIVE** – To investigate whether during distress the fetus mounts a hormonal stress response and its relation with maternal cortisol level and mode of delivery in otherwise uncomplicated pregnancies. **METHOD** – A prospective non-randomized study of 50 neonates of different period of gestation born after acute fetal distress were evaluated for cortisol levels (Study group) in the cord vein and artery, maternal vein and neonatal vein at  $6 \pm 1$  hours of age. They were matched with 50 neonates showing no signs of fetal distress (control group). Data was analyzed by the students t-test, chi-square test, Z-test and Karl Pearson's coefficient of correlation. **RESULT** – The overall cortisol levels did not show any significant difference in cord artery and vein and in maternal vein and neonatal vein at 6 hours after birth in the study and the control groups ( $p$  value  $> 0.10$ ). The maternal cortisol values were consistently higher than the cord serum values. The cortisol levels in cord blood and maternal vein were comparable in distressed and non-distressed fetuses after vaginal delivery but cord serum cortisol was significantly higher in distressed fetuses after cesarean section (CS) than that in the controls. The cortisol levels in neonatal vein at  $6 \pm 1$  hours were significantly higher in distressed fetuses undergoing vaginal delivery in the study group than those in fetuses in the control group ( $p$  value  $< 0.01$ ). The cord blood cortisol levels were significantly higher in study and control group after vaginal delivery than after CS. The maternal and neonatal cortisol values were comparable in both the groups irrespective of the mode of delivery. **CONCLUSION** – Fetal asphyxia and labor trigger a rapid increase in the secretion of stress hormones in the fetus. Mothers respond independently and irrespective of the mode of delivery.

**Key words** : maternal cortisol, cord blood cortisol, neonatal cortisol, fetal distress

### Introduction

The adrenal glands play an important role in the body's defense mechanism against stress in adults. It is commonly believed that fetal pituitary and adrenal glands have a plausible role in initiating labor<sup>1</sup>. At term, fetal adrenal cortisol induces fetal maturity and stimulates the release of estrogen leading to events culminating in labor and delivery<sup>2</sup>. Fetal hypoxia triggers a more rapid increase in stress hormones mainly corticotropin and cortisol. However, the relationship between maternal and fetal cortisol in acute fetal distress is ill defined.

The determination of cortisol concentration in maternal vein, cord blood and neonatal vein is an objective means of assessing intrapartum events and newborn condition<sup>3</sup>. Hence, this study was planned to evaluate the effects of intrapartum stress sufficient to cause infants to have been characterized as having acute fetal distress, on the maternal and fetal cortisol concentrations.

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### Material and Methods

A prospective non-randomized study of 50 women with acute fetal distress was conducted for a period of one year between 1999 and 2000. The study was approved by the hospital ethical committee and an informed consent was obtained from each patient. All the 50 neonates were considered to have suffered intrapartum distress (study group) if any one of the following features seen clinically; tachycardia (heart rate  $> 160$ /min in the absence of maternal tachycardia), bradycardia ( $< 100$ /min baseline heart rate), fresh meconium staining of liquor in fetuses with cephalic presentation and apgar score of neonate at one minute  $\leq 6$ .

The neonates of complicated pregnancy with complications were excluded from the study. The exclusion criteria were pregnancy induced hypertension (PIH), intrauterine growth retardation, malpresentation, antepartum hemorrhage, medical disorders like diabetes mellitus, bronchial asthma, infections like TORCH and hepatitis. Women receiving steroids for pulmonary maturity were also excluded. Fifty matched neonates without fetal distress and their mothers formed the control group. Blood samples for cortisol estimation were taken at the time of delivery from the umbilical artery and vein and from maternal vein. Neonatal samples for cortisol levels at 6 hours after delivery were taken from the peripheral vein. Cortisol was estimated by ELISA / competition test principle.

Results of various group were analyzed by students t-test, chi-square test and Z-test. Karl Pearson's coefficient was used to evaluate the correlations.

## Results

In our study, 58% v/s 44% of all women assessed, presented between 20 to 25 years of age and 24% v/s 36% between 26 to 35 years of age in the study group and control group respectively. The mean age of presentation was 25.16 years in the study group and 26.6 years in the control group. Primigravidas constituted 52% of the cases with a mean gestation of 37.8 weeks in the study group and 44% with a mean gestation of 38.1 weeks in the control group. Further, 72% v/s 54% had CS and 28% v/s 46% had vaginal delivery in the study group and control group respectively.

### Cortisol Evaluation

The maternal cortisol values were consistently higher than the cord serum values (Table I). A statistically significant and positive correlation between levels in maternal vein v/s umbilical artery and vein was seen in both the study group and control group (Fig 1,2,3 and 4). The values of cortisol were comparable in cord

artery and vein in both the groups.

### Cortisol concentration after vaginal delivery

The cortisol levels were compared in 14 and 23 women having vaginal delivery, in the study group and the control group respectively (Table II) and the values of distressed and non-distressed fetuses did not show any significant difference. The maternal cortisol levels were comparable in women with vaginal delivery of distressed and non-distressed fetuses. The neonatal venous sample at 6 hours of age showed significant ( $p < 0.01$ ) higher values of cortisol in distressed fetuses, than non-distressed fetuses delivered vaginally.

### Cortisol levels after cesarean section (CS)

Thirty-six women in the study group underwent CS for fetal distress and 27 in the control group had CS for indication other than fetal distress (Table III). The cord serum cortisol levels were significantly higher (vein- $p < 0.05$ ; artery -  $p < 0.01$ ) in distressed than in non-distressed fetuses delivered by CS. The maternal cortisol values of distressed fetuses were not different from those of the non-distressed fetuses. The neonatal cortisol of distressed and non-distressed babies born after cesarean section demonstrated no significant difference.

**Table I: Comparison of Cortisol Levels ( $\mu\text{g/dl}$ ) in Cord Artery, Cord Vein, Maternal Vein and Neonatal Vein at  $6 \pm 1$  Hours of Age, in Study Group and Control Group**

Sample	Cortisol levels		p-value
	Study group n=50	Control group n=50	
Maternal vein	23.20 $\pm$ 8.09	23.48 $\pm$ 7.61	> 0.10
Cord artery	15.76 $\pm$ 9.84	14.00 $\pm$ 7.70	> 0.10
Cord vein	16.14 $\pm$ 8.34	13.95 $\pm$ 8.01	> 0.10
Neonatal vein	19.17 $\pm$ 9.96	16.18 $\pm$ 6.22	> 0.10

**Table II: Comparison of Cortisol Levels ( $\mu\text{g/dl}$ ) in Study Group and Control Group in Women Undergoing Vaginal Delivery**

Sample	Cortisol levels		p-value
	Study group N=14	Control group n = 23	
Maternal vein	26.45 $\pm$ 7.19	23.56 $\pm$ 8.19	> 0.10
Cord artery	21.44 $\pm$ 6.02	9.97 $\pm$ 5.80	> 0.10
Cord vein	22.48 $\pm$ 4.30	19.39 $\pm$ 7.37	> 0.10
Neonatal vein at $6 \pm 1$ hours of age	20.34 $\pm$ 4.95	15.23 $\pm$ 4.10	<0.01

**Table III – Comparison of Cortisol Levels (µg/dl) in Study Group and Control Group in Women Undergoing Cesarean Section**

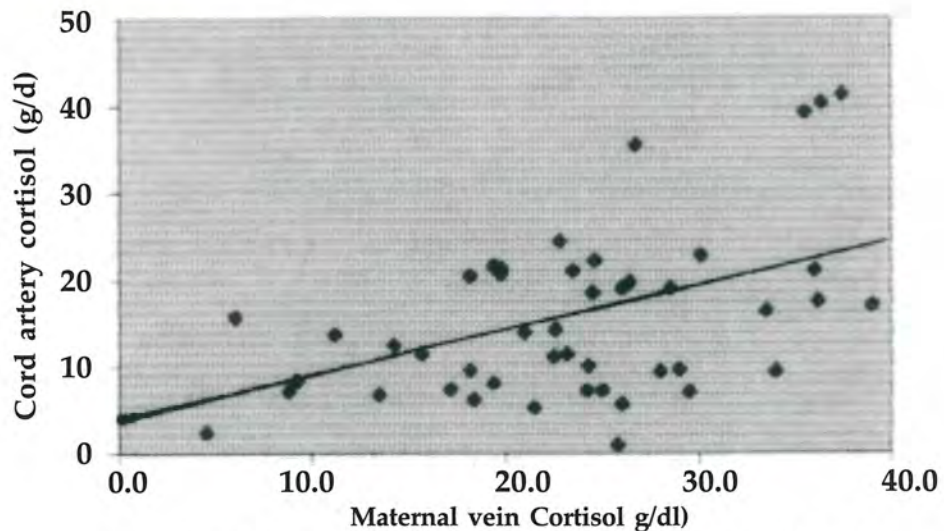
Sample	Cortisol levels		p-value
	Study group N=36	Control group n=27	
Maternal vein	21.94 ± 8.06	23.42 ± 7.07	> 0.10
Cord artery	13.54 ± 10.14	8.91 ± 5.00	<0.05
Cord vein	13.67 ± 8.23	9.31 ± 5.09	<0.01
Neonatal vein at 6 ± 1 hours of age	18.72 ± 7.26	17.00 ± 7.47	>0.10

**Table IV : Comparison of Cortisol Levels (ug/dl) in Relation to Mode of Delivery in Study Group**

Sample	Cortisol levels		p-value
	Cesarean section N=36	Vaginal delivery n=14	
Maternal vein	21.94 ± 8.06	26.45 ± 7.19	<0.10
Cord artery	13.54 ± 10.14	21.44 ± 6.02	<0.01
Cord vein	13.67 ± 8.23	22.48 ± 4.30	<0.01
Neonatal vein	18.72 ± 7.26	20.34 ± 4.95	>0.01

**Table V – Comparison of cortisol levels (ug/dl) in Relation to Mode of Delivery in Control Group**

Sample	Cortisol levels		p-value
	Cesarean section n=27	Vaginal delivery n=23	
Maternal vein	23.42 ± 7.07	23.56 ± 8.19	>0.10
Cord artery	8.91 ± 5.00	19.97 ± 5.80	<0.01
Cord vein	9.31 ± 5.09	19.39 ± 7.37	<0.01
Neonatal vein	17.00 ± 7.47	15.23 ± 4.10	>0.10



**Fig. 1 : Correlation between cortisol levels in maternal vein with cord artery in study group**

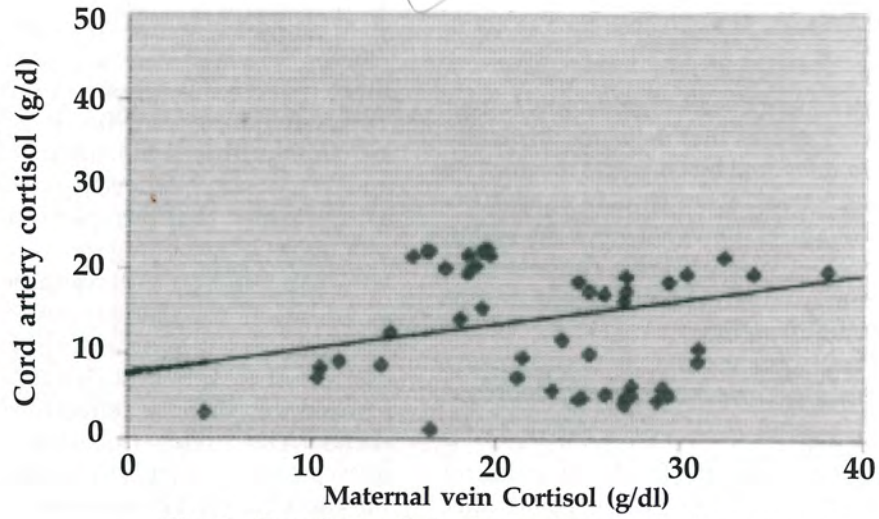


Fig. 2 : Correlation between cortisol levels in maternal vein with cord artery in control group

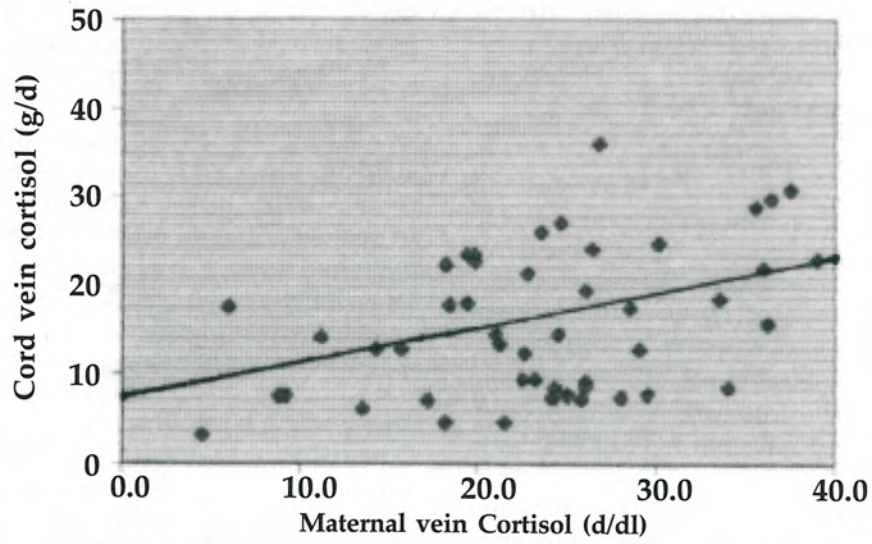


Fig. 3 : Correlation between cortisol levels in maternal vein with cord vein in study group

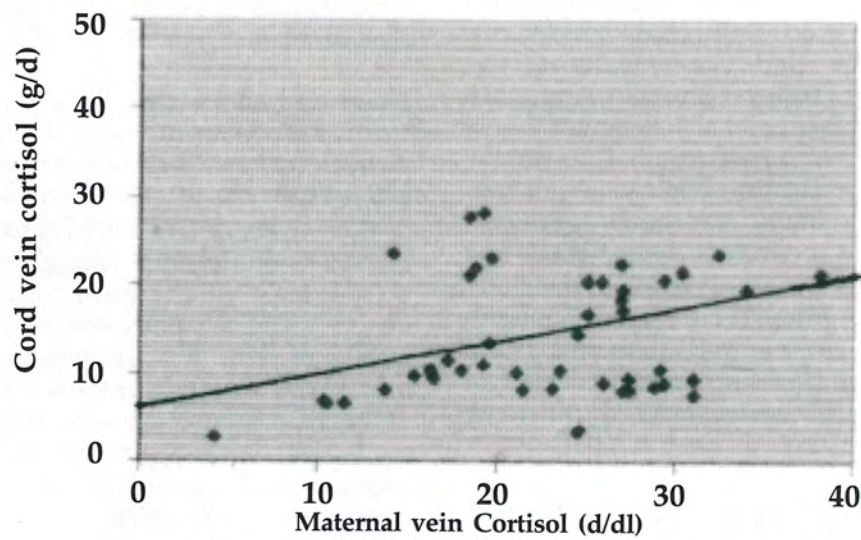


Fig.4 : Correlation between cortisol levels in maternal vein with cord vein in control group

*Comparison of cortisol levels in vaginal delivery vs CS in distressed fetuses*

The cord blood cortisol levels were significantly higher ( $p < 0.01$ ) in distressed fetuses that delivered vaginally ( $n=14$ ) than in those delivered by CS ( $n=36$ ) (Table IV). The maternal cortisol levels were similar in both the groups of distressed fetuses delivered vaginally and of nondistressed ones delivered by CS. The neonatal cortisol samples were comparable in both the groups irrespective of the mode of delivery.

*Comparison of cortisol after vaginal delivery v/s CS in non-distressed fetuses*

Table V shows that the cord serum levels of the control group were significantly higher ( $p < 0.01$ ) in babies after vaginal delivery ( $n=23$ ) than in those of babies after CS ( $n=27$ ). The serum concentrations of maternal cortisol were not significantly different in babies delivered either by vaginal route or by cesarean section. The neonatal venous sample of cortisol showed no significant difference with the mode of delivery.

**Discussion**

Seventy-two percent of women underwent cesarean section in the study group because of early detection of fetal asphyxia and early intervention. The overall cortisol levels in both the groups were significantly higher in maternal venous sample as compared to cord arterial, venous and neonatal venous samples. This is probably attributed to increased corticosteroid binding globulin (CBG), increased rate of production and decreased rate of clearance in pregnant women<sup>4</sup>. Corticotropin releasing hormone (CRH) is released from placenta mainly into maternal circulation at term pregnancy before labor, which causes a surge in maternal cortisol concentration<sup>5</sup>. CRH is bound to a carrier protein in umbilical cord blood, which limits its biologic effects in fetal circulation. The relative immaturity of fetal hypothalamopituitary adrenal axis which matures at 6 months of age after birth and deficiency of 3-beta hydroxy steroid dehydrogenase required for cortisol synthesis could be responsible for low values of cord blood cortisol<sup>1</sup>. In our study, statistically significant correlation was found between maternal venous and cord arterial and venous cortisol levels in the study group and the control group. There was no significant difference in cortisol levels in cord artery and vein in both the groups due to transplacental transfer of maternal cortisol, which overshadowed any difference between the two<sup>4</sup>.

The cortisol levels in cord artery and vein were higher in fetuses of vaginal delivery than those of cesarean section in the study group and the control group. Ikeno

et al<sup>6</sup> suggested that the adrenal response of the fetuses delivered vaginally was greater than that of those delivered by cesarean section. De Amici et al<sup>7</sup> documented the same findings indicating that these are stress-induced elevations of cortisol. Reissland and Wandinger<sup>8</sup> reported similar results. Parker et al<sup>9</sup> concluded that intrapartum stress acutely alters fetal adrenal steroidogenesis. It was proposed that fetal distress (short term compromise of uteroplacental or umbilical cord blood flow) caused an increase in cortisol. They reported highest cortisol levels in distressed infants that delivered vaginally and the lowest levels in those delivered by CS. The cord blood cortisol was higher in distressed than that in non-distressed babies of CS in our study. Distressed babies mount a hormonal response to adapt to the stress stimulus. Bird et al<sup>10</sup> concluded that a surge in cortisol levels is an endocrinal adaptation to delivery related stress. The result of the study of Chelmiki et al<sup>11</sup> indicated that cortisol levels were higher in emergency CS than in elective CS.

Our study indicated that vaginal delivery of distressed and non-distressed fetuses evoke a similar response of cortisol concentration. Labor triggers a rapid increase in the secretion of stress hormones, which is an important maturational stimulus to prepare the fetus for extrauterine survival. Ruth et al<sup>5</sup> also failed to show any significant difference in cortisol levels between the distressed and non-distressed fetuses.

The maternal levels of cortisol were quite comparable in both the study group and the control group as both vaginal delivery and operative abdominal delivery are stressful to the mother. Gitau et al<sup>12</sup> documented that maternal cortisol values were similar in cesarean section and vaginal delivery group while stress experienced by fetus caused a variation in cord blood cortisol concentration.

There was no statistically significant increase in cortisol levels in the neonatal venous sample in distressed fetuses than that in non-distressed fetuses delivered by CS; this was because of early detection of fetal distress and intervention for better fetal outcome<sup>4</sup>. On the other hand, significant difference was noted in distressed fetuses than in non-distressed fetuses delivered by vaginal delivery. It may be the result of the response to intrapartum stress leading to higher concentration of cortisol. Posaci et al<sup>13</sup> studied 64 women with term pregnancies and established that method of delivery affects acid-base and hormonal status of human fetus evoking higher cortisol levels in acidemic group.

Thus in fetal distress, the fetus produces cortisol levels

by itself, independent of the mother. Maternal cortisol levels are triggered by labor and are not affected by the mode of delivery.

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