



ISSN NO. 2320-5407

Journal homepage: <http://www.journalijar.com>

INTERNATIONAL JOURNAL
OF ADVANCED RESEARCH

RESEARCH ARTICLE

To study the effect of mode of delivery on umbilical cord cortisol level.

Dr. Sameer P Darawade,¹ Dr Sandhya V Haribhakta², Dr. Dhananjay D Vaze³, Seema G⁴, Dr. Shilpa A. Pratinidhi^{5*}

1. Associate Professor, Department of Obstetrics and Gynecology, Smt. Kashibai Navale Medical College and General Hospital. Pune
2. Assistant Professor, Department of Paediatrics, MIMER Medical College and Dr BSTR hospital. Talegaon(D).
3. Assistant Professor, Department of General Surgery, Smt. Kashibai Navale Medical College and General Hospital. Pune.
4. Consulting Biochemist, Delhi
5. Professor and Head, Department of Biochemistry,⁵ MIMER Medical College and Dr BSTR hospital. Talegaon(D).

Manuscript Info

Manuscript History:

Received: 14 November 2015
Final Accepted: 22 December 2015
Published Online: January 2016

Key words:

Cortisol, Newborn, Mode of delivery.

*Corresponding Author

Dr. Sameer P Darawade

Abstract

perinatal stress and pain. The mode of delivery results in specific amounts of cortisol in blood samples taken from the umbilical cord immediately at birth. Stress of cortisol may trigger HPA axis which may have repercussions later in life as infants develop.

Aims and Objectives: To study the response of umbilical blood cortisol and anthropometry in newborns with respect to mode of delivery that is Cesarean section (CS) and Vaginal delivery.

Materials and Method: The study was conducted between July 2014 and March 2015, written consent was obtained from 35 pregnant subjects at the time of admission to the ward, were divided into two groups based on mode of delivery, vaginal delivery and section, and blood cortisol was analysed on cord blood sample at the SKNMC and General Hospital, Pune.

Result: Out of total 35 newborns were studied there was no significant difference in anthropometry parameters like age, weight, head circumference, chest circumference, length, abdominal circumference, however the levels of cortisol were significantly more in vaginal delivery 356.92 (± 188.27) ng/ml as compared with caesarean section. 164.87 (± 113.24) ng/ml (P value = 0.002)

Conclusion: Human fetus mounts a cortisol response during the partition and this response is highest during the section as compared to the vaginal delivery. The cortisol may trigger HPA axis which may have repercussions in adult life.

Introduction: Cortisol is released in response to

Copy Right, IJAR, 2016., All rights reserved

INTRODUCTION

Cortisol is glucocorticoid class of hormone, and is produced in humans by the zona fasciculata of the adrenal cortex within the adrenal gland.[1] It is released in response to stress and low blood-glucose concentration. There is increasing evidence that perinatal stress and pain can have a long term effects [2,3,4]. Birth is a process which is most stressful experience undergone by most babies. [5]. It is well known that parturition is associated with a large increase in the levels of fetus stress hormones such as cortisol and catecholamines [6,7,8] Birth is a painful process for the mother and that during the late gestation fetus is able to feel pain, birth may be painful to the fetus.[5] Several studies have shown that caesarean section (CS) are less painful to the fetus than the spontaneous vaginal

deliveries, in which cord blood cortisol, beta endorphin and catecholamines levels are much lower.[9-13] The hormones present in the fetal circulation have a few main sources. hormones in fetal plasma may be derived from circulating precursor molecules by fetal or placental tissues metabolism [14,15], nutritional challenges increase catabolic hormone concentrations (e.g. cortisol). [14,15,16] Glucocorticoid concentrations in the fetus throughout most of the gestation period are low and are derived from the mother following maternofetal concentration gradient. This transplacental concentration gradient is maintained by placental enzyme 11b-hydroxysteroid dehydrogenase type 2 (11b-HSD-2) which plays a pivotal role in controlling fetal exposure to high levels of maternal glucocorticoid by converting cortisol into its inactive metabolite, cortisone. [14,15,17-20] This enzyme is the key factor in limiting fetal and placental exposure to maternal glucocorticoids. [21,22,23] Once the fetal adrenal cortex is activated in late gestation, the fetus becomes the primary source of circulating glucocorticoids. The result is a progressive increase in both: the basal cortisol levels and the adrenocortical responsiveness to adverse conditions.[14,16,24] Increased fetal glucocorticoid exposure can therefore occur as a result of increased maternal cortisol levels, decreased placental 11b-HSD-2 activity or increased cortisol output by the fetal adrenal. The mode of delivery results in specific amounts of cortisol in blood samples taken from the umbilical cord immediately at birth. [25-29]

We planned to undertake the study in order to find out whether there is any difference in the levels of cortisol in full term infants with respect to mode of delivery.

Objectives:-

1. To study the response of umbilical blood cortisol in newborns with respect to mode of delivery that is Cesarean section (CS) and Vaginal delivery.
2. To study anthropometry in newborns delivered by Cesarean section (CS) and Vaginal delivery.

Materials and Method:-

This research was granted ethics approval by the institutional ethical committee. The study was conducted between July 2014 and March 2015, written consent was obtained from 35 pregnant subjects at the time of admission to labor and delivery at the SKNMC and General Hospital, Pune. No attempt was made to assess ethnicity or socioeconomic status. The catchment area for this hospital was predominantly middle class and suburban.

Consent addressed access to labor and delivery chart records and approval for additional umbilical cord blood sampling, immediately after the standard clinical practice of obtaining umbilical cord samples for to quantify corticosteroid hormones was obtained. All newborns were delivered in term, vaginally, in less than 8 hours from the beginning of the active phase of the first stage of delivery, and between 8 The gestational age was calculated according to the first day of the last menstrual period and was corrected by ultrasonic assessment when a discrepancy exceeded one week. In all cases APGAR score was rated as greater or equal to eight in the first and fifth minute.

Multiple pregnancies, pregnancies complicated by preeclampsia or diabetes, stillborns and malformed newborns were excluded from the study. Tobacco, alcohol, or medications other than ferrous sulfate during pregnancy were not taken. Other deliveries were included in the study. Care was taken to see that vasoactive and analgesic drugs were not administered to the mother in the labor before delivery of the fetus. The data of maternal age and parity, gestational age, newborns gender and birthweight were collected during and after delivery. 2 ml of cord blood samples were taken from the umbilical vein into plain tubes immediately after newborns delivery when the umbilical cord was clamped and before delivery of the placenta.

Samples were immediately refrigerated, and allowed to stand for at least one hour before being centrifuged (4000 G for 5 min). Serum was separated, stored at 2–8°C and afterwards all samples were analyzed all at the same time for serum cortisol levels, using automated Immuno analyser, Mini Vidas® at Department of Biochemistry, SKNMC and GH, Pune. Results were coded by author and hormone analyses in the research setting were blind to patient name and mode of delivery.

Result:-

A total of 35 newborns were studied, they were divided into two groups those delivered by vaginal delivery and those delivered by section,

Table 1 illustrates the anthropometry study between both the groups.

The mean age of mothers in case of vaginal delivery was 22.9 years as compared to caesarean section which was 23.7 years , statistically this was not significant.

Mean weight of new borns in case of vaginal delivery was 2659 grams as compared to caesarean section which was 2680 grams, statistically this was not significant.

Head circumference of new borns in case of vaginal delivery was 34.7 cms as compared to caesarean section which was 35 cms , statistically this was not significant.

Chest circumference in case of new borns in case of vaginal delivery was 32.9 cms as compared to caesarean section which was 33.1 cms , statistically this was not significant.

Length of new born in case of vaginal delivery was 44.6 cms as compared to caesarean section which was 46.7 cms , statistically this was not significant.

Abdominal Circumference of new borns in case of vaginal delivery was 26.4 cms as compared to caesarean section which was 26.2 cms , statistically this was not significant.

Table no 1 : Comparision of Anthropometry details of new borns.

Sr No	Age (Years)	Weight (Grams)	HC (Cms)	CC (Cms)	Length (Cms)	Abd Circum (Cms)
Vaginal Delivery	22.9 (± 3.49)	2659 (± 380)	34.7 (± 2.7)	32.9 (± 2.07)	44.6 (± 3.4)	26.4 (± 2.5)
Caesarean Section	23.7 (± 3.19)	2680 (± 450)	35 (± 2.7)	33.1 (± 2.6)	46.7 (± 2.9)	26.2 (± 1.98)
P Value	NS	NS	NS	NS	NS	NS

Table 2:- Comparision of Cortisol details of new borns.

Sr No	Umbilical Cord blood Cortisol
Vaginal Delivery (n=27)	356.92 (± 188.27) ng/ml
Caesarean Section(n=8)	164.87 (± 113.24) ng/ml
P Value	0.002 (less than 0.01, so significant)

If P is <0.001 it is significant.

Table 2 Illustrates the comparison of level of cortisol in both the groups. The level of umbilical cord blood cortisol in case of Vaginal Delivery was 356 ng/ml compared to Caesarean Section which was 164 ng/ml. this figure was statistically significant .

FIGURE 1 : SCATTER DIAGRAM OF DISTRIBUTION OF CORTISOL

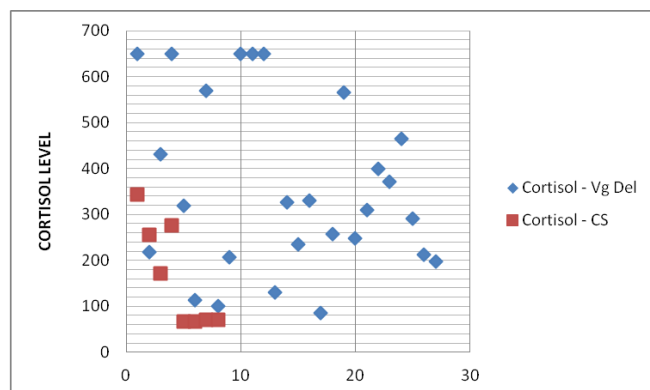


Figure 1 shows the scatter distribution of cortisol (ng/ml) levels in both the groups.

DISCUSSION:

Cortisol hormone is secreted from Zona Fasciculata of the adrenal cortex. Its level in new born is different depending from the mode of delivery is the most important factor, particularly vaginal versus caesarean. We have used mixed blood and there have been various other studies which have used mixed or venous cord blood, which contains a higher percentage and varying proportions of maternal cortisol. This could be an impounding factor. Although we cannot exclude a maternal cortisol contribution (indeed there will be a component), This has demonstrated that it is not just the final passage down the birth canal that raises cortisol, but that contractions themselves which stresses the fetus and raises the cortisol levels. [30]

Birth is a stressful event and there are significant changes in the hormonal profile associated with parturition, particularly in the stress-related hormones. Plasma concentrations of catecholamines in both the fetus (predominantly norepinephrine) and mother (predominantly epinephrine) are markedly elevated during labor and delivery [31,32,33]. It is thought that the characteristic elevation in the concentration of catecholamine in cord blood after an uncomplicated vaginal birth (typically 10–15 times higher than that observed in a resting adult) is advantageous to both the birthing fetus and newly born infant. A surge in catecholamines promotes normal breathing, increases blood flow to the heart and brain, mobilizes fuel, and increases infant alertness [32]. Whereas extremely high concentrations of catecholamines in cord blood are associated with severe oxygen deprivation to the fetus, no surge at all is associated with low Apgar scores [32]. This is a concern for infants born by elective cesarean delivery because they do not typically have an increase in catecholamine concentrations; infants born of mothers who begin labor but end with a cesarean delivery have catecholamine concentrations higher than those born by an elective cesarean, but lower concentrations than those born by vaginal delivery [33,34]. Other hormones reportedly affected by the birth process include prolactin, insulin, adrenocorticotropin, and cortisol [33,35,36]. In a study of 51 mother-infant pairs, free cortisol concentrations were significantly higher in both mothers and infants at term in 21 cases of fetal distress (persistent bradycardia resulting in vacuum or forceps delivery) than in 30 cases of uncomplicated vaginal delivery. [36] In our study, cortisol level was statistically highly significant in CS when compared to full term vaginal delivery. From the level of cortisol we can conclude that, there is a highly complex process involving the interaction of metabolic hormones and their roles in the regulation of glucose homeostasis, weight gain and growth of newborns whether preterm or full term babies. As the time duration of vaginal delivery is longer than cesarean delivery, the neonate born by vaginal delivery is subjected to under more stressful conditions before birth. The cortisol level was affected by low pH, maternal gravidity or parity, and vaginal delivery, which indicates that physiological responses are necessary to adapt to the changes in intrauterine circumference from the fetal period to the neonatal period [38]. According to Chernukha et al, in the course of vaginal delivery, maternal cortisol level increases significantly, the rise being higher in parturients with growth retarded fetuses [39]. The corticotropin-releasing hormone concentrations may enhance the predictive value of midgestational maternal corticotrophin releasing hormone as a screening parameter for the prediction of preterm birth. [40].

Maternal cortisol level may play an important role in intrauterine brain development (evaluated by head circumference of the neonates) [41]. Stress also adversely affects milk volume and delays lactogenesis; it has also been shown by animal studies that perinatal stress results in long term programming of the hypothalamic-pituitary-adrenal axis. In humans, birth is the major stressor in the perinatal period and caesarean delivery before labour is known to lower the degree of infant stress, as reflected by cord cortisol concentrations.

Summary and Conclusion:

Finally to conclude that, human fetus mounts a cortisol response during the delivery and this response is highest during the section as compared to the vaginal delivery. This stress of cortisol may trigger HPA axis which may have repercussions later in life as infants develop. More detailed studies are needed. Small sample size was a major limitation of this study, we plan to undertake a bigger study, including study on maternal blood glucose concentrations, simultaneous maternal cortisol concentrations and new borns feeding behaviors as well.

Acknowledgement:

We express our deep gratitude to all who consented to volunteer in this project. We acknowledge and indebted to the research facilities provided by SKNMC and GH Pune 41 (Maharashtra), India. We also thank Dr Mrs PR Naphade, Prof and Head Department of Obstetrics and Gynaecology, Dr MV Hegde Prof and Head, Dept of Biochemistry and their supporting staff for procurement and processing of the samples and Mrs Aparna Sagare who guided me for statistical data analysis.

REFERENCES:

1. "Cortisol and Stress: How to Stay Healthy". About.com. Retrieved 2011-11-29. <https://en.wikipedia.org/wiki/Cortisol> □ Scott E (2011-09-22).
- 2 Rachel Gitau, Esse Menson, Victoria Pickles, Nicholas M.Fisk,Vivette Glover, Neil Mac Lachlan. Umbilical cortisol levels as an indicator of the fetal stress response to assisted vaginal delivery. European Journal of Obstetrics and Gynecology and Reproductive Biology 98 (2001) 14-17.
3. Meaney M, Bhatnagar S. Diorio J et al. Molecular basis for the development of individual differences in the hypothalamic – pituitary adrenal stress response. Cell Mol Neurobiol 1993; 13: 321-47.
4. Clarke AS, Schneider ML. Prenatal stress has long term effects on behavioural responses to stress in juvenile rhesus monkeys. Dev Psychobiol 1993;26:293-304.
5. Taddio A, Katz J, Ilersich AL, Koren G. Effect of neonatal circumcision on pain response during subsequent routine examination. Lancet 1997;349:599-603.
6. Glover V, Fisk N. Fetal pain: implications for research and practice. Br J Obstet Gynaecology 1999;106:881-6.
7. Padbury JF, Roberman B, Oddie TH, Hobel CJ, Fisher DA. Fetal catecholamine release in response to labour and delivery. Obstet Gynaecol 1982;60:607-11.
8. Economides DL, Nicolaidis KH, Linton EH. Plasma cortisol and adrenocorticotropic in appropriate and small for gestational age fetuses. Fetal Therapy 1988;3: 158-64.
9. Falconer AD, Poyser IM. Fetal sympatho-adrenal mediated metabolic responses to parturition. Br J Obstet Gynaecol 1986;93:747-53.
10. Facchinetti F, Lanzani A, Genazzani AR. Fetal intermediate lobe is stimulated by parturition. Am J Obstet Gynecol 1989;161: 1267-70.
11. Ruth V, Hallman M, Laatikainen T. Corticotrophin-releasing hormone and cortisol in cord plasma in relation to gestational age, labor and fetal distress. Am J Perinatol 1993;10:115-8.
12. Bird JA, Spencer JA, Mould T, Symonds ME. Endocrine and metabolic adaptation following caesarean section or vaginal delivery. Arch Dis Child Fetal Neonatal Ed 1996;74:F132-4.
13. Gitau R, Cameron A, Fisk NM, Glover V. Fetal exposure to maternal cortisol. Lancet 1998;352:707-8.
14. Fowden AL, Forhead AJ. Endocrine mechanisms of intrauterine programming. *Reproduction* 2004; 127: 515–526.
15. Fowden AL, Ward JW, Wooding FPB, Forhead AJ, Constancia M. Programming placental nutrient transport capacity. *J Physiol* 2006; 572: 5–15.
16. Fowden AL, Forhead AJ. Endocrine mechanisms of intrauterine programming. *Reproduction* 2004; 127: 515–526.
17. Parker CR, Favar JK, Carden LG, Brown CH. Effects of intra-partum stress on fetal adrenal function. *Am J Obstet Gynecol* 1993; 169: 1407–1411.
18. Seckl JR. Prenatal glucocorticoids and long-term programming. *Eur J Endocrinol* 2004; 151: 49–62.

19. Seckl JR, Meaney MJ. Glucocorticoid programming and PTSD risk. *Ann N Y Acad Sci* 2006; 1071: 351–378.
20. Clarke KA, Ward JW, Forhead AJ, Giussani DA, Fowden AL. Regulation of 11b-hydroxysteroid dehydrogenase type 2 activity in ovine placenta by fetal cortisol. *J Endocrinol* 2002; 172: 527–534.
21. Seckl JR. Prenatal glucocorticoids and long-term programming. *Eur J Endocrinol* 2004; 151: 49–62.
22. Seckl JR, Meaney MJ. Glucocorticoid programming and PTSD risk. *Ann N Y Acad Sci* 2006; 1071: 351–378.
23. Clarke KA, Ward JW, Forhead AJ, Giussani DA, Fowden AL. Regulation of 11b-hydroxysteroid dehydrogenase type 2 activity in ovine placenta by fetal cortisol. *J Endocrinol* 2002; 172: 527–534.
24. Challis JR, Sloboda D, Matthews SG *et al.* The fetal placental hypothalamic-pituitary-adrenal (HPA) axis, parturition and post natal health. *Mol Cell Endocrinol* 2001; 185: 135–144.
25. Gitau R, Menson E, Pickles V, Fisk NM, Glover V, MacLachlan N. Umbilical cortisol levels as an indicator of the fetal stress response to assisted vaginal delivery. *Eur J Obstet Gynecol Reprod Biol* 2001;98:14-7.
26. Mears K, McAuliffe F, Grimes H, Morrison JJ. Fetal cortisol in relation to labour, intrapartum events and mode of delivery. *J Obstet Gynaecol* 2004;24:129-32.
27. Vogl SE, Worda C, Egarter C, *et al.* Mode of delivery is associated with maternal and fetal endocrine stress response. *BJOG* 2006;113:441-5.
28. Miller NM, Fisk NM, Modi N, Glover V. Stress responses at birth: determinants of cord arterial cortisol and links with cortisol response in infancy. *BJOG* 2005;112:921-6.
29. Bird JA, Spencer JA, Mould T, Symonds ME. Endocrine and metabolic adaptation following caesarean section or vaginal delivery. *Arch Dis Child Fetal Neonatal Ed* 1996;74:F132-4.
30. RCOG 2005 *BJOG: an International Journal of Obstetrics and Gynaecology* 112, pp. 921–926.
31. Goldkrand JW, Schulte RL, Messer RH. Maternal and fetal plasma cortisol levels at parturition. *Obstet Gynecol* 1976;47:41– 45.
32. Fernando R, Bonello E, Gill P, Urquhart J, Reynolds F, Morgan B. Neonatal welfare and placental transfer of fentanyl and bupivacaine during ambulatory combined spinal epidural analgesia for labour. *Anaesthesia* 1997;52:517 –524.
33. Fisk NM, Gitau R, Teixeira JM, Giannakouloupoulos X, Cameron AD, Glover VA. Effect of direct fetal opioid analgesia on fetal hormonal and hemodynamic stress response to intrauterine needling. *Anesthesiology* 2001;95:828 –835.
34. van den Berg A, van Elburg RM, van Geijn HP, Fetter WP. Neonatal respiratory morbidity following elective caesarean section in term infants. *Eur J Obstet Gynecol Reprod Biol* 2001;98:9– 13.
35. Wolkowitz OM, Epel ES, Reus VI. Stress hormone-related psychopathology: pathophysiological and treatment implications. *World J Biol Psychiatry* 2001;2:115– 143.
36. N.M. Miller, a N.M. Fisk, a N. Modi, b V. Glover. American Society for Clinical Nutrition Stress responses at birth: determinants of cord arterial cortisol and links with cortisol response in infancy. . *Am J Clin Nutr* 1998;68:335–44.
37. Adham Hegazy, Maha Awadalla, Salwa El-Batrawy, Abeer Abdel-Mageed and Ahmed Eleswed. Amyline Hormone, Leptin and Other Metabolic Hormones in Preterm Babies Research Journal of Medicine and Medical Sciences, 2009; 4(2): 415-420.

38. Takashi Imamura, Maki Sato¹, Koichi Hashimoto , Tsutomu Ishii, Aya Goto, Hayato Go, Tsutomu Kwarada, Yukihiro Kawasaki, Nobuo Momoi, Niro Ujiie, Keiya Fujimori, & Mitsuaki Hosoya. Glucocorticoid receptor expression and cortisol level in cord blood of term Infants. *The journal of maternal –fetal and neonatal medicine* , Nov 2011 ;24(11): 1312-1316.
39. Chernukha EA, Komissarova LM, Malysheva VA, Abubakirova AM, Galstian AA. Cortisol contents in maternal and umbilical artery blood during delivery of low birth weight fetuses. *Akush Ginekol (Mosk)* 1989; (1): 26-30 (Russian)
40. Siler-Khodr TM, Forthman G, Khodr C, Matyszczyk S, Khodr Z, Khodr G. Maternal serum corticotropin-releasing hormone at midgestation in Hispanic and white women. *Obstet Gynecol* 2003; 101: 557-64.
41. Karamizadeh Z, Saki S, Kashef. Comparison of Umbilical Cord and Maternal Serum Levels of IGF- Leptin and Cortisol in Appropriate for Gestational Age and Small for Gestational Age Neonates. *Int J Endocrinol Metab* 2008; 2: 89-94.