INTRODUCTION

Corticotrophin releasing hormone (CRH) is released from the hypothalamus in response to stress. In primates, it is also produced by placenta. In the second half of pregnancy, there is great increase in maternal CRH blood level. The role of CRH in pregnancy is not clear but it is believed to function in initiation of parturition and regulation of foetal development.

The rising level of placental CRH as gestation advances causes a change in foetal Cortisol concentrations, foetal lung maturation, amniotic fluid proteins, phospholipids, and myometrial receptor expression, which combine, through a set of independent activating pathways, to precipitate labour and delivery.

It is suggested that CRH may influence the development of foetal central nervous system and its organization in the last two trimesters of pregnancy. High levels of CRH lead to an increase in foetal Cortisol level via positive feedback loop. This results in damage to the pyramidal cells of hippocampus and a further increase in CRH level. CRH may then act on parahippocampal and limbic areas and acts as a neurotoxin. Damage to these areas may have adverse effects on the development of the fetus.

Foetal exposure to Glucocorticoids and CRH has both beneficial and detrimental consequences for foetal growth and maturation.

Exposure to cortisol in the last trimester is critical for the maturation of foetal systems like cardiovascular, urinary, respiratory and over foetal growth. Women who use synthetic cortisol during pregnancy are more likely to deliver infants with foetal growth restriction and low birth weight. Similarly, exposure to CRH at 33 weeks gestation has been associated with foetal growth restriction.

APGAR score was developed in 1952, by Dr. Virginia APGAR to evaluate the condition of neonates born at hospitals. This simple system is based on a sum of five numbers obtained 60 seconds after birth. The numbers are determined by objective observations of five signs (heart rate, respiratory effort, reflex irritability, muscle tone, and colour), each of which can be determined easily and without interfering with the care of the neonate.

Ballard newborn maturity rating and classification chart is widely used indicator of post delivery gestational age and has been to assess development. It measures six aspects of neuromuscular maturity (posture, square window of wrist, arm recoil, popliteal angel, scarf sign, and heel to ear) and six aspects of physical maturity (skin lanugo, body hair shed after birth, planter surface of foot, breasts, eye/ear, and genitals.

Present study was conducted to find the relation of CRH level on the overall development of foetus.
MATERIAL AND METHODS

Present study was conducted in the Department of Physiology, Isra University Hyderabad, and its clinical laboratory in collaboration with Liaquat University of Medical and Health Sciences Hospital Hyderabad, and Countess of Dufferin Fund Hospital Hyderabad. Fifty healthy women with singleton intrauterine pregnancy in 31–34 weeks of gestation were recruited from the antenatal clinics. Mean age of the women was 23.88±4.01 years.

Women with twin or multiple pregnancies, chronic hypertension, chronic heart or renal disease, endocrine disorders, history of foetal congenital or chromosomal anomalies, abnormalities of uterus and cervix were excluded from this study. Smokers and steroid user were also excluded.

Personal information of every individual was recorded on a specifically designed questionnaire after obtaining the informed consent. This was followed by thorough clinical examination.

Gestational age was determined by physical examination, date of last menstrual period and ultrasound data. All subjects were followed until delivery.

Neonatal evaluations were done by APGAR score and Ballard newborn maturity rating score.

Plasma CRH level was determined by enzyme immunoassay by commercially available kit EIA-1631 Manufactured by DRG International Inc., USA.

RESULTS

Results are summarised in Table-1–4 and Figure-1–4. 7 subjects were lost to follow-up.

Table-1 shows subject distribution according to CRH level. According to CRH level, subjects were divided into 4 groups. Table-2 shows that mean CRH value in all subjects was 50.03±9.33 ng/ml. The mean APGAR score in the same subjects was 7.60±0.49. Table-3 shows that mean Ballard score in all subjects was 41.70±3.13. Mean Neuromuscular maturity score in the same subjects was 19.51±3.23 and the mean physical maturity score was 22.86±1.56. Table-4 shows CRH wise distribution of mean Ballard Score. There was a significant difference among the mean Ballard score of each group.

Figure-1 shows correlation between CRH and Ballard score. There is a negative correlation between CRH and Ballard score with r value of -0.801 (p<0.001). Figure-2 shows correlation between CRH and Physical maturity score. There was a negative correlation between physical maturity and CRH (r=-0.47). Figure-3 shows correlation between CRH and neuromuscular maturity score. There was a negative correlation between CRH and neuromuscular maturity with r value of -0.56. Figure 4 shows correlation between CRH and APGAR score. There was no significant correlation between these two parameters.

Table-1: Distribution of subjects according to mean CRH value

<table>
<thead>
<tr>
<th>Group</th>
<th>CRH ng/ml</th>
<th>n=43</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Less than 40 ng/ml</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>41–50 ng/ml</td>
<td>18</td>
</tr>
<tr>
<td>3</td>
<td>51–60 ng/ml</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>61–70 ng/ml</td>
<td>5</td>
</tr>
</tbody>
</table>

Table-2: CRH value and Mean APGAR score in all subjects (n=43)

<table>
<thead>
<tr>
<th>Variable</th>
<th>n=43</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corticotropin-Releasing Hormone (CRH) ng/ml</td>
<td>50.03±9.33</td>
</tr>
<tr>
<td>APGAR score</td>
<td>7.60±0.49</td>
</tr>
</tbody>
</table>

Table-3: Ballard Score, Mean neuromuscular score, and Mean Physical maturity score of all subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>n=43</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Ballard Score</td>
<td>41.70±3.13</td>
</tr>
<tr>
<td>Neuromuscular maturity Score</td>
<td>19.51±3.23</td>
</tr>
<tr>
<td>Physical maturity Score</td>
<td>22.86±1.56</td>
</tr>
</tbody>
</table>

Table-4: CRH wise distribution of Mean Ballard Score

<table>
<thead>
<tr>
<th>Group</th>
<th>CRH</th>
<th>n</th>
<th>Ballard Score</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;40</td>
<td>5</td>
<td>45.0±0.8</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>41–50</td>
<td>18</td>
<td>43.6±0.0</td>
<td>0.01*</td>
</tr>
<tr>
<td>3</td>
<td>51–60</td>
<td>15</td>
<td>39.8±1.65</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>4</td>
<td>61–70</td>
<td>5</td>
<td>38.0±0.01</td>
<td>0.05***</td>
</tr>
</tbody>
</table>

Results are expressed as Mean±SD

*p value is statistically significant – between groups 1 and 2

**p value is statistically significant – between group 2 and 3

***p value is statistically significant – between group 3 and 4

Figure-1: Correlation between CRH values and Ballard Score

DISCUSSION

CRH is a peptide hormone released from hypothalamus during stress. Its levels are undetectable in men and non-pregnant women. It levels increase tremendously during pregnancy, especially in the last trimester. This signifies that it has a definite role in pregnancy/labour.

In the present study we estimated the level of plasma CRH at 31–33 weeks of gestation in normal pregnant women. These women were followed till delivery and at birth assessment of foetal maturation were done by Ballard and APGAR scores.

Of the many functions assigned to CRH during pregnancy one is that it is involved in the development and maturation of the fetus.  

CRH stimulates the secretion of glucocorticoids via ACTH. Foetal exposure to glucocorticoids and CRH has both beneficial and detrimental consequences for foetal growth and maturation. Exposure to cortisol in the last trimester is critical for the maturation of foetal systems like cardiovascular, urinary, respiratory and over all foetal growth. Women who use synthetic cortisol during pregnancy are more likely to deliver infants with foetal growth restriction and low birth weight. Similarly, exposure to CRH at 33 weeks gestation has been associated with foetal growth restriction.

In the present study, level of CRH showed a significant inverse or negative correlation with Ballard score, neuromuscular maturity, and physical maturity.

High levels of CRH are associated with low Ballard score. Ellaman et al reported that increased CRH at 31 week was significantly associated with decrease in physical and neuromuscular maturation. Each unit increase in maternal CRH (pg/ml) was associated with a 0.06 decrease (p<0.001) in total Ballard score.

Posen found an inverse correlation between CRH level and neuromuscular maturity but found no correlation of CRH with physical maturity.

CRH may influence the development of foetal central nervous system and its organisation in the last two trimesters of pregnancy. High levels of CRH with associated rise in cortisol result in damage to the hippocampus, parahippocampal and limbic areas.

APGAR score was within normal limits and showed no significant correlation with CRH.

It has been observed that there are considerable variations in assigning APGAR score, and it has poor interobserver reliability.
CONCLUSION
CRH and Glucocorticoids are needed for the development and maturation of foetus at specific windows of intrauterine life. Increased level of both hormones is harmful at times when these are not required in abundance.

REFERENCES

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