

Study the Effect of Some Hormones on Type of Labor

Rafeda M.AL-Amiri (1) Hanaa S.Khadum (2) Awatif H.Issa (3)

(1) Basrah University /College of Dentistry /Department of Basic Science

(2)(3) Basrah University/College of Science/ Department of Pathological Analysis

Abstract:

Background: Labor is the process by which the fetus is expelled from the uterus; it requires regular, effective contractions that lead to dilation and effacement of the cervix. Endocrine changes during pregnancy female sex hormones (Estrogen, Progesterone, and human Gonadotrophin). These hormones are responsible for most of the physiologic changes during pregnancy and labor, and other hormones such as Oxytocin, Prolactin, and Leptin. **Method:** A (4ml) blood sample was collected by test tubes were used and then serum for measuring the hormones by ELISA. **Results:** Oxytocin hormone was significantly increased in caesarean section group; Hormones have no significant differences in age with birth type. And caesarean section obese group showed a significantly lower level of oxytocin.

Conclusion: we conclude that the Oxytocin hormone was increased in the caesarean section group and serum Oxytocin level decreased with the increase of body mass index, there is an inverse correlation between Oxytocin and Leptin hormones in the three groups of delivery.

Keyword: caesarean section, labor, sex hormones, Oxytocin and Leptin

Corresponding Author mrs.fateh@yahoo.com

INTRODUCTION

Pregnancy is the most important event in the life of any female organism to reproduce its progeny. It is a very coordinated process among the mammalian species involving reproductive organs and hormones (Rahman 2006). Labor is a clinical diagnosis. The onset of labor is defined as regular, painful uterine contractions resulting in progressive cervical effacement and dilatation. Cervical dilatation in the absence of uterine contraction suggests cervical insufficiency, whereas uterine contraction without cervical change does not meet the definition of labor (Wei *et al.*, 2015). Labor is the process by which the fetus is expelled from the uterus. More specifically, it requires regular, effective contractions that lead to dilation and effacement of the cervix (Liao *et al.*, 2005). Overall, consistent and coherent evidence from physiologic understandings and human and animal studies find that the innate hormonal physiology of childbearing has significant benefits for mothers and babies. (Buckley 2016).

Endocrine changes during pregnancy female sex hormones (i.e., estrogen, progesterone, and human gonadotrophin) are secreted primarily by the placenta. These hormones are responsible for most of the physiologic changes during pregnancy and labor (Fox, 2011), and other hormones such as Oxytocin, Prolactin, and Leptin. Labor can be divided into three types: Normal labor, Induced labor and caesarean section.

Normal labor a spontaneous vaginal delivery (SVD) occurs when a pregnant female goes into labor without the use of drugs or techniques to induce labor (Koc *et al.*, 2013). Caesarean sections defined as the use of surgery to deliver one or more babies.

Oxytocin is a hypothalamic neuropeptide first recognized as a regulator of parturition and lactation which has recently gained attention for its ability to modulate social behaviors. (Mitre *et al.*, 2017). The precise role of oxytocin in human labor remains a controversial and unresolved issue. Historically oxytocin was assumed to be the initiating factor of parturition, Oxytocin and the oxytocin receptor have two important roles in labor at some stage of the labor process, and

elevated plasma oxytocin is observed in all placental mammals (Blanks and Thornton 2003).

Prolactin is synthesized in the front lobe of pituitary by the lactotroph cells, and secretion is controlled by a complicated hormone system which includes inhibiting and stimulating factors (Hoak 1988 and Dimitraki *et al.*, 2016). Our own in vitro studies have suggested a role for Prolactin and also human chorionic gonadotropin in the secretion of Prostaglandin by the fetal membranes that are associated with the regulation of labor. Thus, phasic changes in maternal Prolactin during this time may represent an important endocrine event in the initiation and/or the progression of labor (Fernandes *et al.*, 1995). A recent study has indicated that Prolactin inhibits Prostaglandin production from the human fetal membranes (Tyson *et al.*, 1985). Prolactin levels are reduced significantly in both amniotic fluid and decidua after the onset of labor, thus providing evidence for a role of Prolactin in human parturition (Kinoshita *et al.*, 1991).

Leptin is a peptide hormone primarily secreted by adipose tissue. In non pregnant humans, it plays a key role in body fat and energy expenditure regulation. Leptin deficiency is associated with anovulation and infertility, however, pregnancy in a woman with a leptin-receptor mutation has been reported (Maguire *et al.*, 2012 and Nizard *et al.*, 2012). Maternal serum leptin levels increase and peak during the second trimester and plateau until term in concentrations two to four times higher than those in non pregnant women. This increase is only partially due to pregnancy weight gain, because leptin also is produced in significant amounts by the placenta (Maymó *et al.*, 2011). The main physiological regulator of body weight is leptin, leptin acts as an adiposity signal in negative feedback loop that regulates food intake and energy expenditure may due to leptin binding to specific receptors in different areas of the hypothalamus (Khan *et al.*, 2012 and Jin *et al.* 2000) has been detected leptin receptor in various tissues of the reproductive axis such as pituitary gonadotrope cells, granulosa, theca and ovary cells (Karlsson *et al.*, 1997); endometrium (Kitawaki *et al.*, 2000), and this explain how the leptin can exert its effects on the reproductive hormone. It regulates food intake, body adiposity, and reproductive competence. Nutrients, hormones, and neurotransmitters also seem to play a major role in the regulation of leptin expression and secretion (Cammisotto *et al.*, 2003).

Fang *et al.*, (2001) found that there are three naturally types showing estrogen in women, β -estradiol, estriol, and estrone. The estrogen mainly promotes proliferation and growth of specific cells in the body that is responsible for the development of most secondary sexual characteristics of the female (Guyton and Hall, 2006). During pregnancy, tremendous quantities of estrogens are also secreted by the placenta; only three estrogens are present in significant quantities in the plasma of the human female: β -estradiol, estrone, and estriol (Mesiano, 2017). The large amount of estrogens which also secreted by the placenta during pregnancy (Guyton, 2001).

The progestin function mainly to prepare the uterus for pregnancy and the breasts for lactation (Guyton and Hall, 2006). The progesterone secreted in significant amounts only during the latter half of each ovarian cycle, when secreted by the corpus luteum in the normal no pregnant female. Also, the tremendous amount of progesterone was secreted by the placenta during pregnancy. (Guyton, 2001). The role of the sex steroid hormones is clear, progesterone inhibits and estrogen promotes the events leading to parturition.

The aim of the study

Since the rate of caesarean section increased in previous years. This study aims to research on the causes of increased incidence of obstetrics labor in women and the increasing rate of cesarean deliveries at present time and clarifying the role of hormones between the two groups of women who deliver by normal and caesarean section. Therefore the study is designed to achieve the following objectives: Measurement the level of Oxytocin, Progesterone, Estrogen Leptin and Prolactin hormones). Because they are considered important factors on the delivery, we want to know whether these factors influence the determination of the type of birth in women who have a normal delivery or caesarean section.

Ethics and Consent

Informed consent was obtained from all patients, and their identities remained anonymous during the entire study process.

Materials and Methods

This is a cross-sectional study carried out at Al-Basrah Teaching Hospital for Maternity and Childhood in Basrah city of Iraq from October 2017 until February 2018. An 86 pregnant female were included in this study (32) were delivered by caesarean section, (29) by normal delivery and (25) by induced labor. A (4ml) blood sample was collected from each pregnant female at the time of admission by test tubes were used and then left for some short time to let blood clot and then serum samples were obtained by centrifugation at room temperature at 3500 rpm for 10 minutes for measuring the hormones by ELISA. Statistical package for social science (SPSS) version 20 was used to analyze the data T-test.

Study Design

Women were divided according to their ages into three groups. The first group was 18-25 years, the second group was 26-32 years and the third group was 33-40 years. BMI was calculated as $\text{Body Mass Index} = \text{Weight (kg)} / \text{height (m}^2\text{)}$. Pregnant women were divided into three groups, normal ($\leq 25\text{kg}$), overweight (25-30kg) and Obese ($\geq 30\text{kg}$). Gestational age was determined as the period from the date of the woman's last menstrual period, and correlated with ultrasound reports that pregnant women had.

Results

As shown in table (1), it appeared that Oxytocin hormone was significantly increased in caesarean section group, while Prolactin, Progesterone, and Leptin hormones were not significantly decreased in caesarean section group in comparison with induced and normal labor groups. On the other hand, data referred that Estrogen also not significantly decreased in the normal group in comparison with induced and caesarean section groups.

Table (1): Hormonal parameters of normal labor, induced labor and caesarean section regardless of age and BMI categories.

Variables	Normal Labor N=29	Induced Labor N=25	Caesarean Section N=32	P.Values
Oxytocin	369.84±22.11	367.32±21.04	427.81±16.01	0.048*
Prolactin	146.67 ± 29.43	140.16 ± 31.05	135.96 ± 34.5	0.43
Progesterone	74.97 ±5.75	76.37 ± 3.07	73.01± 8.48	0.14
Estrogen	2723.5 ±401.09	2853.8 ± 130.53	2845.5 ±80.8	0.09
Leptin	522.5 ±360.6	597.7 ±357.0	512.6± 293.5	0.6

(*) mean significant, P value <0.05. The value was expressed as (mean ± SD).

Caesarean section A3 group showed no significant higher level of Oxytocin but induced labor A3 group showed no significant lower level of prolactin and leptin in comparison with normal labor and caesarean section but it appeared no significantly higher level of progesterone. While no significant variation was recorded in the level of estrogen between normal, induced and caesarean section A3 group Table (2).

Table (2): Hormonal parameters of, normal labor, induced labor and caesarean section groups. (Ages ≤ 25 years, Ages 26-33years and Age ≥ 34 group).

Parameters	Normal Labor N=29			Induced Labor N=25			Caesarean Section N=32			P Values
	Age ≤ 25 Years groupA1 (N= 19)	Age 26- 33 Years groupA2 (N= 6)	Age ≥ 34 Years groupA3) (N= 4)	Age ≤ 25 Years groupA1 (N=19)	Age 26- 33 Years groupA2 (N= 3)	Age ≥ 34 Years groupA3 (N= 3)	Age ≤ 25 Years groupA1 (N=13)	Age 26- 33 Years groupA2 (N=14)	Age ≥ 34 Years groupA3 (N= 5)	
Oxytocin	349.58 $\pm$ 24.24	417.67 $\pm$ 41.99	389.30 $\pm$ 51.42	357.85 $\pm$ 27.49	389.12 $\pm$ 59.38	389.71 $\pm$ 59.38	422.60 $\pm$ 29.69	440.02 $\pm$ 28.52	408.55 $\pm$ 46.00	0.917
Prolactin	146.290 $\pm$ 7.593	143.114 $\pm$ 13.151	153.705 $\pm$ 16.107	135.538 $\pm$ 7.390	168.851 $\pm$ 18.599	141.031 $\pm$ 22.779	131.774 $\pm$ 8.934	134.230 $\pm$ 8.609	151.593 $\pm$ 14.406	0.583
Progesterone	74.501 $\pm$ 1.482	77.997 $\pm$ 2.638	72.659 $\pm$ 3.231	76.389 $\pm$ 1.482	76.069 $\pm$ 3.731	76.541 $\pm$ 3.731	71.271 $\pm$ 1.792	74.844 $\pm$ 1.727	72.440 $\pm$ 2.890	0.884
Estrogen	2762.71 $\pm$ 58.899	2548.51 $\pm$ 102.016	2809.51 $\pm$ 124.943	2860.67 $\pm$ 57.328	2823.64 $\pm$ 144.272	2834.07 $\pm$ 176.696	2859.80 $\pm$ 69.306	2825.61 $\pm$ 66.785	2864.40 $\pm$ 111.752	0.744
Leptin	549.086 $\pm$ 78.740	429.136 $\pm$ 140.118	536.691 $\pm$ 171.609	644.106 $\pm$ 78.740	472.774 $\pm$ 198.157	429.040 $\pm$ 198.157	491.169 $\pm$ 95.192	558.737 $\pm$ 91.729	439.664 $\pm$ 153.492	0.767

The value was expressed as (mean $\pm$ SD).

As shown in (Table 3) in the comparison between normal, induced and caesarean section groups, it appeared that normal labor normal weight group showed a significantly higher level of oxytocin and caesarean section overweight group showed a significantly higher level of oxytocin, while a caesarean section obese group showed a significantly lower level of oxytocin in comparison with normal and induced labor obese group.

Table (3): Hormonal parameters of, normal labor, induced labor and caesarean section groups. According to different body mass index categories.

Parameters	Normal Labor N=29			Induced Labor N=25			Caesarean Section N=32			P Value
	Normal weight (≤ 24.9) (N=1)	Over weight (25-29.9) (N=6)	Obese (≥ 30) (N=22)	Normal weight (≤ 24.9) (N=2)	Over weight (25-29.9) (N=5)	Obese (≥ 30) (N=18)	Normal weight (≤ 24.9) (N=1)	Over weight (25-29.9) (N=9)	Obese (≥ 30) (N=22)	
Oxytocin	452.6 $\pm$ 38.83	428.03 $\pm$ 67.21	347.27 $\pm$ 20.26	443.5 $\pm$ 95.04	409.10 $\pm$ 42.51	346.96 $\pm$ 25.40	436.65 $\pm$ 20.26	432.8 $\pm$ 35.92	197.8 $\pm$ 95.04	0.03*
Prolactin	154.6 $\pm$ 6.80	151.04 $\pm$ 31.17	118.10 $\pm$ 12.72	167.28 $\pm$ 22.04	140.73 $\pm$ 7.56	127.35 $\pm$ 13.94	139.57 $\pm$ 10.39	135.83 $\pm$ 6.64	105.72 $\pm$ 31.17	0.149
Progesterone	71.29 $\pm$ 6.50	77.01 $\pm$ 2.65	74.58 $\pm$ 1.38	77.19 $\pm$ 4.60	77.19 $\pm$ 2.91	76.04 $\pm$ 1.53	76.68 $\pm$ 6.50	70.68 $\pm$ 2.16	73.80 $\pm$ 1.38	0.579
Estrogen	2897.82 $\pm$ 240.60	2448.56 $\pm$ 98.22	2793.75 $\pm$ 52.50	2868.69 $\pm$ 170.13	2881.97 $\pm$ 107.60	2843.80 $\pm$ 58.35	2894.97 $\pm$ 240.60	2851.34 $\pm$ 80.20	2840.95 $\pm$ 51.29	0.112
Leptin	225.8 $\pm$ 337.06	390.08 $\pm$ 137.60	572.17 $\pm$ 71.86	500.2 $\pm$ 238.34	462.11 $\pm$ 150.74	646.24 $\pm$ 79.44	374.58 $\pm$ 337.06	390.4 $\pm$ 112.35	568.97 $\pm$ 71.86	0.994

The value was expressed as (mean $\pm$ SD).

Discussion

The result of the present study showed that the caesarean section group had significantly higher Oxytocin concentration than induced and normal labor groups. However, many studies are known about the role of this hormone during pregnancy and labor. Several studies concerning Oxytocin in pregnancy and labor have been published (Fuchs, *et al.*, 1984, Gintzler and Liu, 2001), this result was agreement with (Risberg, 2009) which she said that the plasma Oxytocin concentration was higher in week 36 than at the beginning of parturition and did not change during the phases of labor. Because of the effects of estrogen, the uterine Oxytocin receptor population density increases progressively during pregnancy to reach a peak at term. Therefore, the uterus becomes very sensitive to the effects of Oxytocin while preparing for parturition. This could explain the increased oxytocin level that was observed in our study (Carvalho *et al.*, 2004).

However, a comparison of three age groups of Caesarean section group (≤ 25 years, 26-33 years and ≥ 34 years), showed no significant differences in all studied parameters which included Oxytocin, Prolactin, Progesterone, Estrogen and Leptin in comparison with three age groups of induced and normal labor groups. The findings of this study agreement with the study of (Velarde and Menon 2016)

In respect of BMI categories the normal labor normal weight category in our results showed the significantly higher level of Oxytocin in comparison with induced labor and Caesarean section BMI categories, however, our data show that serum Oxytocin level decreased with the increase of BMI and vice versa.

Despite the risks and prevalent use of Oxytocin, little is known about the association between oxytocin titration and maternal outcomes across BMI groups (Maeder *et al.*, 2017). In accordions with our study, more recently researchers evaluated Oxytocin requirements across BMI groups and found that oxytocin dosage increases with increasing BMI (Roloff *et al.*, 2015). Women who are obese are more likely to experience poor labor outcomes such as longer length of labor and cesarean birth (Hilliard *et al.*, 2012). The present study demonstrated that the PRL level decreased with the increased BMI.

Our data was agreement with (Buonfiglio *et al.*, 2016) who's suggested that high leptin levels are a possible cause of the peripheral and central PRL resistance presented by obese animals which leads to impaired lactation performance, so they found reduced milk production and offspring viability.

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