IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)
e-ISSN:2278-3008, p-ISSN:2319-7676. Volume 12, Issue 4 Ver. V (Jul – Aug 2017), PP 51-56
www.iosrjournals.org

Levels of Cortisol, Progesterone, Prolactin with Liver Enzymes and Lipid Profile in First Trimester Pregnant Iraqi Women

Prof. Ali Sh.Sultan[1] Noor AlhudaKh Ibrahim[2]Ban H. Hameedi[3*]
Prof.Bushra F. Hasan [4]

[1]*PhD. In Physiological and Reproduction and Hormones/College of Science/University of Al-Mustansiriyah/Iraq*
[2]*MSc in Biochemistry College of Nursing, University of Baghdad, Iraq*
[3]*MSc in Biology College of Nursing, University of Baghdad, Iraq*
[4]*MSc in Biochemistry, College of Science for Women, University of Baghdad, Iraq*
Corresponding author: Ban H. Hameedi

Abstract: *Astudy was conducted to investigate the changes insome hormones, lipid profileand liver enzymes in the first trimester pregnant Iraqi women as compared with the apparently healthy control women. A total of 60 women included30 pregnant women at first trimester selected from women admitted to Gynecology Department at Medical City of Baghdad Teaching Hospital,* all pregnant women aged between (20-35) years*andcompared with30 apparently healthy women. The cortisol, progesterone,and prolactin hormones were measured using BiomerieuxMinividas Model: vidas12, while lipid profile,liver enzymes and some kidney function test (urea,creatinine) were evaluated by colorimetric method using a spectrophotometer.Results showedasignificantincreasing(P<0.01)in cortisol (30.52 ng/ml), progesterone(39.91 ng/ml), and prolactin (72.85 ng/ml) in pregnant women as compared to the corresponding means of 3.80, 0.83, and 22.20 ng/ml in the control group. TheLDL level (99.70 mg/dl) was significantly increased(P<0.01)in pregnant as compared with 71.62 mg/dl in the control ,while HDL was significantly (P<0.01) decreased in the pregnant.*

The level of the ALP, ALT, and AST was significantly lower (P<0.05) in pregnant than control. It was found a positive significant correlation between the three hormones and BMI,HDL whilethe correlations between theses hormones and each of LDL,ALK,ALT and AST were negative.The progesterone and prolactin showed asignificant correlation(P<0.05) with cholesterol.In conclusion: The serum cortisol, prolactin and progesteronewere significantly increased (P<0.05) during pregnancy in comparison with thenon-pregnant group, there was alsoa significant increasing(P<0.05) in cholesterol and LDL in pregnant women, kidneyfunction testsshowed non-significant difference, while liver enzymes were within normal range.

Keywords*:progesterone, Cortisol, Progesterone, Prolactin, Liver Enzymes, Lipid Profile*

Date of Submission: 21-07-2017 Date of acceptance: 05-08-2017

I. Introduction

Many physiological changes are happened in the pregnant woman to demand the developingofafetus, maintain homeostasis and prepare for birth and lactation. Adaptations of pregnant womenresult from the effect of multiple factors, includingthe influences of reproductive hormonescytokines,complementproteins,growth factors, and other signaling proteins (Burton and Jauniauxm, 2004; Fujimori et al., 2015). Biochemicalmeasurements reflect these changes and are clearly distinct from the non-pregnant state. It has been reported that the imbalance in metabolites depends on several reasonsincluding, genetics nutrition, and mother's lifestyle so this changes effected on many body organs, such as kidney and liver(Mohammed et al., 2015; Salih et al., 2016). Many of physiological changes during pregnancy are mediated by hormones. Hormones are responsible for keeping homeostasis, development, regulation of growth, and cellular communication (Sala et al., 1995).The elevated of Adrenocoricotropin (ACTH) stimulates cortisol production by adrenal glands on

pregnancy. The adrenal gland undergoes hypertrophy with increases in the zonafascullta (the portion of the adrenal that produces glucocorticoids such as cortisol). Plasma levels ofthecortisol releasing hormone (CRH) progressively increase during the second and third trimesters of pregnancy (Jung et al., 2011). Circulating cortisol levels regulate carbohydrate and protein metabolism. Total and free cortisol increase 2 to 8 fold. Thus pregnancy is characterized by a transient hypercortisolemia (Nepomnaschy, 2000). A normallyACTH release would turn off when increased cortisol level. Therefore, the increased ACTH with increased cortisol during pregnancy suggests changes in the set point for cortisol release. Thus, in spite of the elevated cortisol and ACTH, physiological responses to stress (such as blood pressure, heart rate, and cortisol reactivity) are maintained during pregnancy (Rajab et al., 2000).In the beginning of pregnancy, theprogesterone is produced by the corpus luteumandlater by the placenta. It maintains the activity of decidual secretory that required for implantation; inhibit prostaglandin production by affecting on uterine smooth muscle to maintain myometrial relaxation.

Progesterone acts on smooth muscle in other organs of the body, especially in the gastrointestinal and renal system (Fucls et al., 2000).Prolactinhormoneisreleased from the anterior pituitary. Its action to increase and mature ducts and alveoli in the breast for lactation after birth (Eriksson et al., 2000). There is a marked increase in prolactin level in pregnancy associated with the effects of angiotensin II, gonadotropin releasing hormone, and vasopressin on the pituitary. As it is known high levels of estrogen in pregnancy inhibit lactation, and this inhibitiondisappearquicklywith removal of the placenta, the major source of estrogen (Sobrinho, 2003).

The renal system undergoes structural and functional changes during pregnancy. Changes in renal function increased the metabolic and circulatory demands of pregnancy. The renal system excretes maternal and fetal waste products. Pressure placed on the renal system and the relaxant effects of progesterone on vascular tissue enhance the ability of the renal system to accommodate the cardiovascular changes of pregnancy (Roberts, 2004). Plasma cholesterol doubles and plasma triglyceride level increases threefold during pregnancy. The lipid content of the low density lipoproteins increases in pregnancy as does high density lipoprotein triglyceride content. Serum lipid levels fall rapidly after delivery, but both cholesterol and triglyceride concentrations remain elevated at 6-7 weeks postpartum. Triglycerides provide maternal fuel and thus save glucose for the fetus. An increase in LDL is due to placental steroidogenesis. Pregnancy results in profound changes in maternal physiology and metabolism (Cekmen et al., 2003). Without a proper knowledge of these changes and the different normal values which are appropriate in pregnancy and which may vary with gestational age, it is impossible to diagnose accurately and manage maternal and fetal disorders (Burton and Jauniaux, 2004). Almost half of the total plasma alkaline phosphatase in pregnancy is placental AP isoenzyme, but bone AP isoenzyme levels are also markedly increased, liver AP isoenzyme level do not change significantly in pregnancy. Serum gamma glutamyltransferase (GGT) and transaminase levels overall are lower in pregnancy than in the non-pregnant adult population. There are no significant gestational changes in GGT, AST or ALT nor during labor or in the puerperium. Bilirubin level remains within normal adult levels during pregnancy(Tran et al., 2016).The aim of the current study is to estimate the level of cortisol, progesterone and prolactin hormones in pregnant women compared to the normal state and evaluate the level of lipid profile, kidney function test and liver enzymes during pregnant compared with non-pregnant women.

II. Materials And Methods

Serum samples include (30) pregnant women and(30) non pregnant women as control group collected from the maternity center of Baghdad teaching hospital in Baghdad medical city between March-November 2016. All pregnant women aged between (20-35) years. (5ml) of blood were obtained from each subjects after overnight fasting by vein puncture , collected and divided into two aliquots, (2ml) in plain tube for(ELIZA) technique, and (3ml) in evacuated plastic tubes for routine work All hormonal analysis was performed at the clinical chemistry laboratory at nursing home hospital. Serum specimens from each woman were assayed in the same laboratory run. Cortisol, progesterone, prolactin hormones were analyzed by enzyme linked immune absorbent assay (ELISA). Serum liver enzymes and lipid profile were measured by commercially available kits and read by colorimetric method by spectrophotometer.Low-Density Lipoprotein (LDL) and very Low-Density Lipoprotein (v LDL) were calculated by the Friedewald formula (Burton and Jauniaux, 2004):

LDL mg/dL = C - HDL - TGS/5

V LDL mg/dL= TGS/5.

Pregnant women with hepatic, diabetes millets, renal, endocrine disease, uncontrolled hypertension, on medications for lowering lipid, and smokers were excluded from the study.

Statistical Analysis

The statistical analysis was performed using SAS program (2012). Unpaired t test was used to assess thedifferencebetweentheparameters. $P < 0.05$ was considered significant.

III. Results

The results showed that the levels of cortisol, progesterone, and prolactin were significantly higher (P<0.05) in pregnant women as compared with control (Table 1).However, no significant difference was detected between two groups in the creatinine and urea (Table 2). The level of the HDL (55.59 mg/dl) was significantly (P<0.05) higher in the control as compared with the pregnant (42.90 mg/dl) while the levels of the LDL and cholesterol were significantly (P< 0.05) higher in pregnant (Table 3). Concerning the liver enzymes, all the levels were significantly (P< 0.05) higher in control compared with pregnant (Table 4). However the mean of age was not significantly (P< 0.05) but the BMI differed significantly (P< 0.05) as the pregnant mean (31.12) was higher than control (26.89)(Table 5). Table (6) shows the correlation between level of hormones and the studied parameters. A significant correlation was found between cortisol, BMI, LDL, HDL and all liver enzymes (p<0.05). Also there is a significant correlation between progesterone level and each of the BMI, LDL, HDL, cholesterol and all liver enzymes (p<0.05) (p<0.01) , while prolactin show significant correlation with BMI, LDL, HDL, cholesterol and liver enzymes (p<0.01) (p<0.05). Table (7) showed the correlation between levels of hormones, which show a significant correlation between cortisol and prolactin and non-significant correlation between progesterone & prolactin and progesterone &cortisol .

Table(1):-Comparison between (cortisol, progesterone, and prolactin,ng/ml) in sera of pregnant and control groups.

Group	Mean ± SD		
	Cortisol (ng/ml)	Progesterone(ng/ml)	Prolactin(ng/ml)
Control (30)	3.80 ± 1.98b	0.83 ± 0.50b	22.20 ± 1.58b
Pregnant(30)	30.52 ± 11.77a	39.91 ± 21.43a	72.85 ± 19.77a
LSD value	4.369 **	11.488 **	7.247 **
(P<0.01).			

Table(2): Comparison between (creatinineandurea,mg/dl) in sera of pregnant and control groups.

Group	Mean ± SD	
	Creatinine (mg/dl)	Urea (mg/dl)
Control (30)	0.846 ± 0.14	14.01 ± 6.16
Pregnant (30)	0.874 ± 0.30	16.73 ± 6.92
LSD value	0.121 NS	6.715 NS

NS: Non- Significant.(P>0.05)

Table(3): Comparison between lipid profile mg/dl in sera of pregnant and control groups.

Group	Mean ± SD				
	LDL mg/dl	VLDL mg/dl	HDL mg/dl	Triglyceride mg/dl	Cholesterol mgldl
Control (30)	71.62 ± 26.59b	21.60 ± 9.58a	55.59 ± 21.09a	108.00 ± 47.92	148.82 ± 39.72b
Pregnant (30)	99.70 ± 26.07a	22.90 ± 6.23a	42.90 ± 6.23b	111.23 ± 32.23	165.16 ± 28.42a
LSD	16.328 **	4.154 NS	8.165 **	20.997 NS	17.749 *

*** (P<0.05), ** (P<0.01), NS: Non-Significant.(P>0.05)**

Table(4): Comparison between liver enzymes (ALP,ALT,AST, U/L) in sera of pregnant and control groups.

Group	Mean ± SD		
	ALP (U/L)	ALT (U/L)	AST (U/L)
Control (30)	89.73 ± 22.94a	20.37 ± 8.73a	22.03 ± 5.78a
Pregnant(30)	6.57 ± 2.80b	7.29 ± 1.03b	13.90 ± 1.90b
LSD value	8.306 **	3.161 **	2.192 **

**** (P<0.01)**

Table (5) :-Comparison in age and BMI between pregnant and control groups **.**

Group	Mean ± SD	
	Age (year)	BMI Kg/m^2
Control (30)	29.96 ± 6.44^a	26.89 ± 2.72^b
Pregnant(30)	30.71 ± 5.41^a	31.12 ± 4.13^a

Means with different letters in the same column significantly different (P<0.01)

Table (6):-Correlation coefficient betweenthe level of (cortisol , progesterone ,prolactin) and other parameters .

Parameter	Correlation coefficient (r)		
	Cortisol	Progesterone	Prolactin
Age	-0.03	-0.07	0.02
BMI	0.58 **	0.27 *	0.32 *
Creatinine	0.08	-0.04	0.05
Urea	0.11	0.08	0.03
LDL	-0.33 **	-0.35 **	-0.44 **
VLDL	0.01	0.03	-0.07
HDL	0.45 **	0.27 *	0.37 **
Triglyceride	0.04	0.06	-0.03
Cholesterol	-0.09	-0.23 *	-0.26 *
ALK	-0.78 **	-0.61 **	-0.81 **
ALT	-0.61 **	-0.48 **	-0.64 **
AST	-0.61 **	-0.45 **	-0.60 **

***(P < 0.05), **(P <0.01)**

Table (7):- Correlation coefficient between levels of hormones

Hormones	Correlation coefficient (r)	Level of Sig.
Cortisol&Prolactin	0.36	*
Progesterone&Prolactin	-0.02	NS
Progesterone&cortisol	0.08	NS
*** (P<0.05), NS: Non-Significant. (P>0.05)**		

IV. Discussion

Many physiological reactions in pregnancy are monitored by hormones produced by the placenta, it acts many roles, the important one is the secretion of steroid hormones, like progesterone and estrogen (Akinloye et al., 2013). Results showed a progressive increasing in the BMI when compared with control groups. This is agreed with other results in which bodyweight progressively elaborated during pregnancy (Ladella et al., 2003; Cornock et al., 2010). Santiago et al., (2001) recorded production of excess amount of prolactin,estrogen, progesterone, and corticosteroids during pregnancy which could influence the various metabolic and endocrine systems (Santiago, 2001). Changes in hormonal level throughout pregnancy have beensubjected to many studies, especially reproductive hormones, which have many conflicting reports explain its changes at each stage of pregnancy.Hormones like progesterone are known to increase progressively during pregnancy. Our result of serum progesterone agreed with previous reports (Eriksson et al., 2000; Fucls et al., 2000). Since progesterone helps to keep integrity of pregnancy, its level increases as the pregnancy progresses. Prolactin level in the current study increased progressively due to the preparing the mammalian gland for postpartum secretion of milk to feed the neonate. The increasing in prolactin level appears to be additional coping strategy for emotional challenges. McLean *et al*(1995) and Sobrinho, (1995), reported that cortisol increasesare related to shock and associated with prolactin and our findings are similar to these results.Sobrinho, (1995) and McLean and Smith, (1995) also reported that prolactin and cortisol are measurable markers of different and alternative strategies to face psychological stress. This may explains the positive correlation observed in the serum cortisol and prolactinlevels in our study.Multiple changes occur in the body's utilization and metabolism of fats duringpregnancy which allow the accumulation of maternal fat stores in the first half of pregnancy and increased fat mobilization in the second half.

These result indicated thatincreasingin lipid profiles may be due to increasing of maternal reliance on fat stores of energy as pregnancy progresses.The current result shows an increasing in the level of many lipoproteins. Thefirst and most dramatically plasma triglyceride levels which was increasedas compared withthenon-pregnant group (Roberts, 2004),while cholesterol containing lipoproteins, phospholipids and fatty acids increased but to a lesser extent than triglycerides. The increasing cholesterol supply is used by the placenta for steroid hormones synthesis. Recent study show that cholesterol and triglycerides correlate positively with progesterone. Similar results were obtained by Parchwani and Patel, (2011) and Ibrahem and Ahmed, (2013) who found significant differences at ($p<0.001$) in the cholesterol, triglyceride, LDL and VLDL in the pregnant women as compared with control group.Although the total cholesterol increased in the third trimester, maximum rate of increase occurred during second trimester (Parchwanii and Patel, 2011). The kidneys are effected during pregnancy. In the early months of pregnancy renal flow is increased nearly by 40% and the kidneys themselves increase in size (1cm). Theurine production is increased to let the endocrine system working properly. The progesterone affects the urinary tract by relaxing the smooth muscles surrounding it, which can often lead to urinary tract infections (UTIs).Ashwood, (1992) reported that pregnancy increases the glomerular filtration rate (GFR) and subsequently increases the clearance of urea and creatinine.However, Tiezts et al., (2000)reported that urea and creatinine levels increased slightly through the last month (four weeks) of pregnancy.In the present study, resultsshowedno significant differences in urea and creatinine in all stages of pregnancy as compared with the control group.The most commonly biomarkers used for liver damage (hepatocellular) are the alanine aminotransferase (ALT) and aspartate aminotransferase (AST), or as they formerly referred to (SGPT) and (SGOT) (Ashwood, 1992).

These enzymes are normally found in the liver cells. They leaks out when liver is injured and take their way to the blood. The ALT is considered to be a more specific marker of liver inflammation, while AST is also found in other organs like the heart and skeletal muscle.The degree of inflammation of liver can be measured by estimation thelevel of theenzymes(ALT) and (AST) (Tiezts et al., 2000; Yonegama and Ikeda, 2000). It is the most useful tests for the routine diagnosis of liver diseases (Ch'nget al., 2005; Guyton and Hall, 2011). The level of serum alkaline phosphatase (ALP) increased mainly during the third trimester of pregnancy. In our study the level of these enzymes found to be within the normal range and no change occurredduring pregnancy.

V. Conclusion

Thepresent study demonstrated the increasing levels of cortisol,progesterone and prolactin hormones in pregnancy.Cholesterol and LDL were increased in pregnant women compared to non-pregnant women. Also there was a significant correlation between cortisol progesterone and prolactin hormoneswithHDL,LDL in pregnant women.

References

[1]. A.G. Guyton, Hall, Text Book of Medical Physiology. 9th ed. W.B. Saunders. Company, 2011.
[2]. A.R. Fucls, O. Behrens, and H. C. Liu, Correlation of nocturnal increase in plasma oxytocin with a decrease in plasma estradiol/progesterone ratio in late pregnancy. Am J Obstet Gynecol,167, 2000, 1559–1563.
[3]. C. Jung, J.T. Ho, D.J. Torpy, A. Rogers, M. Doogue, J.G. Lewis, J. Czajko , and J.R. Inder, A longitudinal study of plasma and urinary cortisol in pregnancy and postpartum, J ClinEndocrinolMetab., 96(5), 2011,1533–1540.
[4]. C.Sala, M. Campise, G. Ambroso, T. Motta, A. Zanchetti, and A. Morganti, A trial natriuretic peptide and hemodynamic changes during normal human pregnancy, Hypertension , 25, 1995, 631-636.
[5]. C.A. Tiezts, W. Burtis, R. Edward, and M. Ashwood, Chemistry of pregnancy".*Clinical Chemistry*, 48, 2000,1740–1741.
[6]. C.L. Ch'ng, M. Morgan, I. Hainsuonth, and J. Kinghom, Prospective study on liver dysfunction in pregnancy in South West Wales, Gut, 21(6), 2005, 876-880.
[7]. D.Parchwanii, and D. Patel, Status of lipid profile in pregnancy, National Journal of Medical Research,1(1), 2011, 2249-4995
[8]. E.R. Ashwood. Evaluating health and maturation of the unborn: the role of the clinical laboratory.Clinical Chemistry, 38, 1992, 1523-29.
[9]. G.J.Burton, and E. Jauniaux, Physiological changes in pregnancy, J Soc. Gynecol Invest, 11, 2004, 342–352.
[10]. Y. Mohammed, H. Damudi, B. Bello, I.S. Yahaya, M.I.S. Musa, and Z.U. Ibrahim, Biochemical assessment of pregnancy-related physiological changes in renal function,American Scientific Research J. for Engineering, Technology, and Sciences , 14(3), 2015, 264-271.
[11]. J. M.Roberts, Pregnancy-related hypertension. In Creasy RK, Resnik R, Iams JD (eds), Maternal-Fetal Medicine. Principles and Practice, 5thedn. Saunders: Philadelphia, 2004.
[12]. K. Rajab, A.M. Mohammad, and F. Mustafa, Increase cortisol in pregnancy, Int J Gynaecol Obstet., 68, 2000, 139–144.
[13]. K. Yonegama K., and J. Ikeda, Changes in maternal bone mineral density during pregnancy and relationship between the density and fetous growth a prospective study, Nippon. Koshu.Eisei, Zasshi, 47, 2000, 661- 669.
[14]. K.G.Nepomnaschy, Cortisol levels and very early pregnancy loss in humans, Endocr .,103, 2000, 3938-3940.
[15]. L. Eriksson , S. Eden, J. Holse, G. Lindstedt, and B. Von Schiltz, Diurnal Variations in thyrotropin, prolactin and cortisol during human pregnancy, Gynecol. Obstet Invest, 27, 2000, 78–83
[16]. L. Eriksson, S. Eden, J. Holse, G. Lindstedt, and B. Von Schiltz, Diurnal variations in thyrotropin, prolactin and cortisol during human pregnancy, Gynecol. Obstet Invest., 27, 2000, 78–83.
[17]. L.Salih L. and M.Mahmood, Quantitative study of some trace elements and blood parameters in the third trimester of Iraqi pregnant women with Pre-eclampsia, Iraqi Journal of Science, 57(3), 2016, 2197-2202.

[18]. L.G.Sobrinho, Prolactin, psychological stress and environment in humans: adaptation and maladaptation. *Pituitary*, 6, 2003, 35-9.
[19]. M. Fujimori, E.L. França, V. Fiorin, C.T. Morais, C. Adenilda, and C. Luiz, Changes in the biochemical and immunological components of serum and colostrum of overweight and obese mothers BMC Pregnancy and Childbirth, 15, 2015,166-172.
[20]. M. McLean, and R. Smith, Cushing's syndrome: how should we investigate in 1995?,The Med J of Austral, 1637, 1995,153-154.
[21]. M.B.Cekmen, A.B. Erbagci, A. Balat, C. Duman, H. Maral, K. Ergen, M. Ozden, O. Balat, and S. Kuskay, Plasma lipid and lipoprotein concentrations in pregnancyinduced hypertension, Clin. Biochem. 36(7), 2003, 575-8.
[22]. O. Akinloye, O. M. Obikoya, A. I. Jegede, D. P. Oparinde, and A. O. Arowojolu, Cortisol plays central role in biochemical changes during pregnancy, International Journal of Medicine and Biomedical Research,2(1), 2013, 3-12.
[23]. R. Cornock, S.C. Langley-Evans, A. Mobasheri, and S. McMullen, The impact of maternal protein restriction during rat pregnancy upon renal expression of angiotensin receptors and vasopressin-related aquaporins, Rep BiolEndocrinol, 8, 2010, 105-116
[24]. S.A.Ibrahem, and S. A. Ahmed, Study of Association between Lipid Profile and Thyroid Hormones in Pregnancy, Journal of Al-Nahrain University, 16 (4), 2013, 37-45
[25]. S.J. Ladella, M. Desai, Y. Cho, and M. G. Ross, Maternal plasma hypertonicity is accentuated in the postterm rat, Am J Obstet Gynecol,189, 2003, 1439-1444.
[26]. T.Santiago, R. Jennifer, S. Michael, and D. Nolled, Sleep and Sleep Disorders in Pregnancy, Gynecol. Obstet Invest,134, 2001, 380–400.
[27]. T.T. Tran, J. Ahn , and N. S. Reau, Clinical Guideline: Liver Disease and Pregnancy, Am J Gastroenterol, 111, 2016,176–194.

IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS) is UGC approved Journal with Sl. No. 5012, Journal no. 49063.

Prof. Ali Sh.Sultan. "Levels of Cortisol, Progesterone And Prolactin with Liver Enzymes And Lipid Profile in First Trimester Pregnant Iraqi women." IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS) 12.4 (2017): 51-56.