

COMPARISON BETWEEN TRIMESTERS: ASSESSMENT OF SERUM NEUROCHEMICAL HORMONES IN NORMAL PREGNANT WOMEN

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ABSTRACT

Although depressive disease is common in pregnant women, but it is always a risk in pregnancy and is tied to a high prevalence of maternal and postnatal mental health issues. The study was performed to compare the concentrations of serum serotonin, ghrelin and γ -aminobutyric acid (GABA) lab tests in third trimester with first trimester and second trimester. The study was performed in 28 pregnant women during their three trimesters as a cross-sectional case control study. Double-blind quantitative determination of serotonin, GABA, and ghrelin concentrations was performed using commercially available competitive enzyme-linked immunosorbent assay (ELISA) kits, according to manufacturer's protocol. The results of the 2nd trimester showed significant raise throughout all hormones when compared to 1st trimester results, and showed the same significance when compared to the 3rd trimesters. On the other hand, the 3rd trimester results showed significant increase level when compared to the 1st trimester except for GABA hormone which increased insignificantly. In conclusion, this study suggested that the 2nd trimester involves in pregnancy-related complication secondary to mood and anxiety problems.

Keywords: serotonin, ghrelin, GABA, trimester, mood, pregnancy

INTRODUCTION

Epidemiological studies have indicated that psychiatric conditions are much more in women compared to men; however, its actual reason is still questionable. Although it is common that ladies are at risk for mood and anxiety problems unusually throughout pregnancy, but then again systematic reports are insufficient on the main reasons behind mood and anxiety problems (O'Connor *et al.*, 2018). Existing reports have estimated the occurrence of pregnant females found with one or more psychiatric disorder between 20% and 30% (Ibanez *et al.*, 2012; Uguz *et al.*, 2018). The incidence of anxiety in pregnancy is not well studied. Several researches have exhibited that maternal stress in pregnancy has an impact on brain structures involved in emotional condition which enable it to cause psychopathology (Tsakiridis *et al.*, 2019). Literature on the incidence of depressive disorders in pregnancy is frequently complicated by the use of various methodologies, protocols and study groups. Controlled studies that systematically measure the direction of depression in pregnancy may arrive at different conclusions (Osborne *et al.*, 2017). Mood alterations are undoubtedly common, due to a combining of hormonal variations with increased tiredness, together with anxiety and sleeping disturbances. Recent studies correlated between lower amounts of allopregnanolone and increased depressive symptoms but other studies finding no relationship. The evidence concerning neurotransmitters and perinatal depression is sparse (Uguz *et al.*, 2018).

Pregnancy is divisible into three time periods, called trimesters, which is a useful way to help describe the changes that take place in times of pregnancy. Many ladies feel in different ways, both of physically and emotionally, during the period of each trimester. A normal pregnancy takes between 37 to 42 weeks, on average forty weeks. The first trimester is week one to week 12, the second is week 13 to week 27, and the third is week 28 to week 40 (Shu *et al.*, 2018).

The aim of this study was to estimate the levels of serotonin, ghrelin and gamma-Aminobutyric acid (GABA) hormones during the three trimesters of pregnant women due to the relation between these hormones and mood. Serotonin (5-HT) and ghrelin are neurotransmitters involved with the regulation of numerous behavioral and mood functions, playing a role in psychological processes in the central nervous system (Wu *et al.*, 2018; Patterson *et al.*, 2010). GABA works as a brake to the excitatory neurotransmitters that cause anxiety (Salazar *et al.*, 2008).

MATERIALS AND METHODS

This research conducted was a cross-sectional case control study. All volunteers participated in the work were in maternal age of 18 to 37 years. Women refused to participate in the study were excluded as well as those with fetal

malformation, multiple pregnancy, severe pregnancy-related complications such as preeclampsia, gestational diabetes mellitus, early membrane rupture, and placental abnormalities affecting fetal growth, also women with severe medical problems such as uncontrolled endocrine abnormalities, cardiovascular and pulmonary system diseases, neurological disease, and metabolic diseases. The study was approved by the ethics committee of Faculty of Medicine of Omdurman Islamic University. Pre-prepared questionnaire including data concerning patients and their pregnancy information (such as age, family history, parity, and BMI) was used. In addition, the objectives and procedures of the study were explained to all participants and written informed consent forms were obtained. The BMI was calculated by dividing the body weight by the square of body height (MacKay, 2010). Venous blood samples were withdrawn from all subjects during the daytime between 9-11 am. 6 ml venous blood was obtained from antecubital vein by standard venipuncture techniques without venous stasis (Nikolac *et al.*, 2013), in SST gel separated serum tubes. Following collection, samples were left to clot, then centrifuged for 5 min at 15000 RPM and serum was separated and stored at - 4°C for less than five days for each patch. All hormones were determined then by the enzyme-linked immunosorbent assay (ELISA) according to manufacturer's protocol. Double-blind quantitative determination of Serotonin, Ghrelin, and GABA concentrations in serum was performed using commercially available competitive ELISA kit. Serotonin (E-EL-0033) and Ghrelin (E-EL-H1919) ELISA kits were obtained from Elabscience, Wuhan, China. While GABA (K7012) ELISA kits were obtained from Immundiagnostik AG, Bensheim, Germany.

Statistical Analysis: All values are mean \pm SD. The level of significance was determined using repeated measures ANOVA followed by Tukey's post-test. $P < 0.05$ was considered significant. For determination of sample size, the level of confidence was set at 95%. The sample size was to range from 15 to 24 for all the parameters. Hence, a sample size of 28 was used.

RESULTS AND DISCUSSION

Pregnancy is a potential stressor and a high-risk period during which women with psychological vulnerability may develop mental health problems. Evidence indicates an increase in psychiatric morbidity particularly anxiety during pregnancy (Moussa and Tayel, 2015).

In the present study, following 28 pregnant women, the second trimester showed the maximum levels in serotonin, ghrelin and GABA hormones, while the first trimester period showed the lowest levels. The 3rd trimester in both serotonin and ghrelin hormones showed significant raised levels ($p < 0.001$) when compared to the 1st trimester results; but showed significant low levels ($p < 0.001$) when compared to the results of the 2nd trimester. Also the mean level of GABA hormone during the 3rd trimester showed significant reduced level ($p < 0.001$) when compared to the 2nd trimester results; but showed insignificant raised level ($p > 0.05$) when compared to the results of the 1st trimester.

These results were disagreed with the study of Adewuya *et al.* (2006) who published that the peak of mood swings appears in the third trimester; and also the results were incompatible with recent study that indicated that neurotransmitters produced and secreted under conditions of increased metabolic demand particularly in the 1st trimester (Almaça *et al.*, 2016). But still most researchers revealed that higher antenatal anxiety is during third trimester of pregnancy when compared to first or second trimester of pregnancy (Priyambada *et al.*, 2017).

Table 1. Demographic, anthropometric, and gestational age of pregnant women.

	1 st trimester (n = 28)	2 nd trimester (n = 28)	3 rd trimester (n = 28)	p value
Age (years)	26.121 \pm 5.94	26.121 \pm 5.94	26.121 \pm 5.94	N/A
Body mass index (kg/m ²)	25.175 \pm 4.44	27.203 \pm 6.12	29.796 \pm 5.87	0.58
Gestational age (weeks)	10.01 \pm 1.00	19.40 \pm 6.22	32.51 \pm 7.84	0.001

All values are mean \pm SD

Table 2. The level of hormones during the trimesters in pregnant women.

Parameter	Pregnancy			LSD _{0.05}
	1 st Trimester	2 nd Trimester	3 rd Trimester	
Serotonin	0.516 ± 0.144 c	1.166 ± 0.378 a	0.801 ± 0.253 b	0.1466
Ghrelin	422.698 ± 77.325 c	721.46 ± 80.398 a	528.838 ± 62.728 b	39.2905
GABA	0.387 ± 0.099 c	0.651 ± 0.1832 a	0.471 ± 0.0754 b	0.0679

All values are mean ± SD, n=28, Similar letters in each row are non-significant according to Duncan Multiple Range Test at p < 0.05.

Contrary to many researchers correlate the severity of anxiety in pregnant women with somatic complaints and obstetric complications that as may be expected to happen in the 3rd trimester and with less usual in the 1st trimester, the result of this research proved that the change of mood hormones was greater in the second trimester of pregnancy period. This result can be concluded that the results of mood hormones during pregnancy are predictive levels. It is also noted that the results of this study showed that hormone levels in the 1st trimester of pregnancy recorded the lowest rate compared to the 3rd and 2nd trimester. On the other hand, since most researches have shown that the second trimester of pregnancy is the least period of mood swings and pregnancy anxiety, this explicitly supports the theory of predictive levels of mood hormones during pregnancy.

Nevertheless, the 28 volunteer women as sample size do not quite enough for generalization of the results of this study. Moreover, due to various exclusions, the findings do not reflect the mood and anxiety disorders among pregnant women in general. There may be various psychosocial factors and other neurochemicals that may contribute to mood swings and anxiety during entire period of pregnancy (McEvoy *et al.*, 2018). A relatively large sample-size and a structured control group are required to strength this study with consideration of parity, multiple pregnancy and gestational complications.

Conclusion

In conclusion, serotonin, ghrelin and GABA hormones were increased significantly in the 2nd trimester compared to 1st and 3rd trimesters. On the basis of our results, we believe that imbalances and fluctuations in these neurotransmitters can cause emotional dysregulation.

Acknowledgement:

The author gratefully acknowledges the Advanced Research Center (ARC labs) for the great helpfulness to run this study.

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(Accepted for publication May 2019)