

## Original Article

**Prediction of Factors Affecting Cognitive Performance in Pregnant Women Using Robust Regression Methods**Adem Doganer<sup>1,\*</sup>, Abdullah Tok<sup>2</sup>, Gulbahtiyar Demirel<sup>3</sup><sup>1</sup>Department of Biostatistics and Medical Informatics, Faculty of Medicine, Kahramanmaraş Sutcu Imam University, Kahramanmaraş, Turkey.<sup>2</sup>Department of Obstetric and Gynecology, Faculty of Medicine, Kahramanmaraş Sutcu Imam University, Kahramanmaraş, Turkey.<sup>3</sup>Department of Midwifery, Faculty of Health Sciences, Sivas Cumhuriyet University, Turkey.

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## ABSTRACT

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**Key words:**Pregnancy;  
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**Introduction:** This study compared the outcomes of cognitive function assessments between pregnant and non-pregnant women groups to demonstrate alterations occurring during pregnancy. Furthermore, we aimed to determine the factors acting on cognitive functions in pregnant women.

**Material and Methods:** 42 pregnant and 42 non-pregnant women were included in the study. In order to compare cognitive performances, Montreal Cognitive Assessment test was applied to women.

**Results:** The assessed scores of cognitive functioning were significantly different between pregnant and non-pregnant women ( $p < 0.001$ ). The test value was obtained as  $22.29 \pm 4.57$  with pregnant women and  $26.02 \pm 2.19$  with non-pregnant women. The cognitive measurements yielded lower scores in the pregnant women. A negative correlation was found between the progesterone hormone levels and cognitive scores ( $p = 0.025$ ). Progesterone hormone, TSH hormone and age of the pregnant were found to be important among the factors affecting the cognitive performances in pregnant women ( $p = 0.04$ ;  $p = 0.001$ ;  $p = 0.033$ , respectively).

**Conclusion:** Significant reductions in cognitive functions are observed in women during pregnancy. During pregnancy, in order to increase the cognitive level of women, hormonal values of pregnant women should be followed.

**Introduction**

The pregnancy process is a complex period in which physiological and sociological changes occur for women (1-4). Physical and mental changes are experienced in women during this period. The pregnancy process should be managed well in terms of adaptation to this period (5-8). The changes

that occur during pregnancy affect women's self-perception and self-esteem (8-11).

Changes in pregnancy alter women's perception of their bodies (12-14). Studies in the literature demonstrate that pregnancy-related changes affect women negatively and this negative perception leads to sexual dysfunction (3,9,11,15). Physical changes during pregnancy (weight

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gain, increases in chest and hip circumferences, changes in skin including hair and nails, etc.) negatively affect the psychology of women (1,4,5). This change causes anxiety and stress by impairing self-esteem in women (8,16,17). During pregnancy, the maternal body develops some adaptation mechanisms to ensure placental blood flow and fetal growth (18-20). Despite these adaptation mechanisms, there is a risk of deficiency in important micronutrients; particularly deficiencies of iron, iodine, folic acid, vitamin D, and vitamin B12 may occur (21-22). These nutrients are involved in biological functions, enzyme activity, signal generation, transcription pathways, and oxidative stress, causing changes in the maternal and fetal metabolism and affecting the mental and emotional well-being (21). Mental and emotional changes occur in women due to hormonal changes developing during pregnancy (13,23). Increased levels of estrogen and progesterone during pregnancy cause hypertrophy and insulin secretion in pancreatic cells; they result in insulin resistance along with the secretion of human placental lactogen, prolactin, and cortisol hormones; they lead to hypertrophy of the thyroid gland, increasing total thyroxine (T4) and total triiodothyronine (T3) levels and lead to hyperplasia and hypertrophy of the parathyroid glands (24). Fatigue, forgetfulness, and mental symptoms may be seen during pregnancy, particularly because of the sedating effects of progesterone on the central nervous system (13,23). In this context, it is suggested that hormonal changes may cause mental fatigue, stress, and forgetfulness in pregnant women, acting on the cognitive perception levels. Regression analysis was

used in the study to determine the factors that affect cognitive scores in pregnant women. When both the dependent and estimator variables are the continuous variables, the linear regression analysis with the least-squares method is used (25). The least-squares method yields erroneous estimations when outliers and extreme observations are present in the data set. The least-squares method is sensitive to extreme values. Using linear regression analysis in such data sets leads to erroneous results. Robust regression methods are preferred for the evaluation of data sets containing outliers. Robust methods provide resistant results in the presence of outliers and allow for obtaining more accurate results compared to linear regression methods. Of the robust methods; least median squares, least trimmed squares, and M-estimators are widely used (26-27).

This study aimed to investigate the effect of changing hormone levels in pregnancy on cognitive perception levels in pregnant women. For this purpose, routinely tested hormone levels and cognitive perception levels of pregnant women were planned to be compared to those of non-pregnant women to investigate any differences between these groups and to examine the effects of progesterone hormone on cognitive scores.

### **Material and Methods**

The study included 42 healthy and non-pregnant women as the control group and 42 healthy pregnant women as the pregnant group. Non-pregnant women were selected from women aged 18-40. Non-pregnant women were selected among women without any cognitive, endocrinal and neurological disorders. The distribution of education levels and locations of non-pregnant women is homogenous.

Participants were randomly selected among volunteers who agreed to participate in the study. The study was conducted on a total of 84 women. Power analysis was utilized to determine the sample size of the study. Based on the power analysis, 84 women were included in the study at an  $\alpha$ -value of 0.05,  $\beta$ -value of 0.20, and a statistical power of 0.80. Equal numbers of pregnant women from 3 different trimester periods were included in the pregnancy group of the study. Before the commencement of the study, approval was obtained from the Clinical Research Ethics Committee of Kahramanmaraş Sutcu Imam University with the registration number of 95 and the decision number of 2018/05-21. The control group of the study was randomly selected among healthy women, who agreed to participate in the study. Eligible pregnant women; who were admitted to the Kahramanmaraş Sutcu Imam University Health Practice and Research Hospital gynaecology and obstetrics outpatient clinic and who attended the follow-up visits regularly, were included in the study on a volunteer basis. The research was conducted between May 2018 and May 2019. Simple random sampling method was used in the selection of the participants. Simple random sampling method was applied based on the sequence numbers of the patients. Volunteers among the pregnant women selected as the sample were included in the study. Sociodemographic information form and the Montreal Cognitive Assessment test (MoCA) were administered to the control group and the pregnant group in the study. Montreal Cognitive assessment was developed by Nasreddine et al. (2005) (28). The test assesses the cognitive dimensions of individuals including attention,

concentration, orientation, abstract thinking, and memory. The Turkish version of the test was developed by Selekler et al. (2010) to score the cognitive functioning (29). The lowest and highest possible score to be obtained from the test are 0 and 30 respectively. High test scores indicate that the cognitive functioning was at high levels and the cognitive functions of the patient were well. Of the pregnant women; who participated in our study, we recorded the gestational week, pregnancy trimesters, supplementary vitamins or drugs used, and the levels of progesterone, ferritin, and TSH.

### **Statistical Analysis**

The conformity of the variables to a normal distribution was tested with the Shapiro-Wilk test. The independent samples t-test was used for comparing the control group and the pregnant women group with normally distributed data. A robust regression analysis was performed to investigate the effects of selected hormones and variables on cognitive levels of pregnant women. Andrew's M-estimator was used for model estimations. Pearson correlation test was used for investigating the relationship between the hormones and sub-dimensions of the cognitive assessment. Statistical parameters were expressed as Mean  $\pm$  SD. Statistical significance level was accepted at a p-value of  $<0.05$ . The study data were analyzed with the IBM SPSS software version 22 (IBM SPSS for Windows version 22, IBM Corporation, Armonk, New York, United States) and R 3.6.0 software.

### **Results**

The mean age of the pregnant women was  $28.10 \pm 5.99$  years. Of the pregnant women, 50% lived in urban areas and 34.1% were university graduates. In the control group;

the mean age was  $27.12 \pm 6.16$  years. Of the women in the control group, 71.4% lived in urban areas and 47.6% were high school graduates.

The mean gestational week of the pregnant women was 22.48. Of the pregnant women, 33.3% had their first pregnancy and 95.2% were not smokers. None of the pregnant women consumed smokeless tobacco products. No medication use history before pregnancy was present in 82.9% of the pregnant women. No medical disorders were present in the medical history of 95.2% of the pregnant women and 73.8% had regular vitamin supplements use during pregnancy. Folic acid was used by 47.5% of the pregnant women.

The comparison of the cognitive assessment scores between the study groups is presented in Table 1. The total scores of the Moca test were statistically significantly different between the control group and the pregnant women group ( $p < 0.001$ ). Cognitive assessment scores of the pregnant women were significantly lower than those of the women in the control group. Similarly, the examination of the cognitive subscales revealed that the visuospatial executive functions and attention scores were statistically significantly different between the pregnant women group and the control group ( $p < 0.001$ ). Sub-parameters of cognitive assessment levels are given in figure 1.

Table 1. Comparison of Cognitive Functions and Cognitive Assessment Score by Groups

	Pregnant (n:42) Mean $\pm$ SD	Control (n:42) Mean $\pm$ SD	p
Visuospatial/Executive	3.64 $\pm$ 1.45	4.57 $\pm$ 0.67	<b>p&lt;0.001*</b>
Naming	2.52 $\pm$ 0.63	2.67 $\pm$ 0.48	0.247
Attention	4.10 $\pm$ 1.61	5.50 $\pm$ 0.89	<b>p&lt;0.001*</b>
Language	2.43 $\pm$ 0.86	2.67 $\pm$ 0.57	0.138
Abstraction	1.45 $\pm$ 0.83	1.88 $\pm$ 0.40	0.003*
Recall	2.64 $\pm$ 1.68	2.90 $\pm$ 1.46	0.448
Orientation	5.88 $\pm$ 0.40	5.83 $\pm$ 0.44	0.602
Cognitive Assessment Score	22.29 $\pm$ 4.57	26.02 $\pm$ 2.19	<b>p&lt;0.001*</b>

Independent samples t test;  $\alpha:0.05$ ;\* Difference is statistically significant

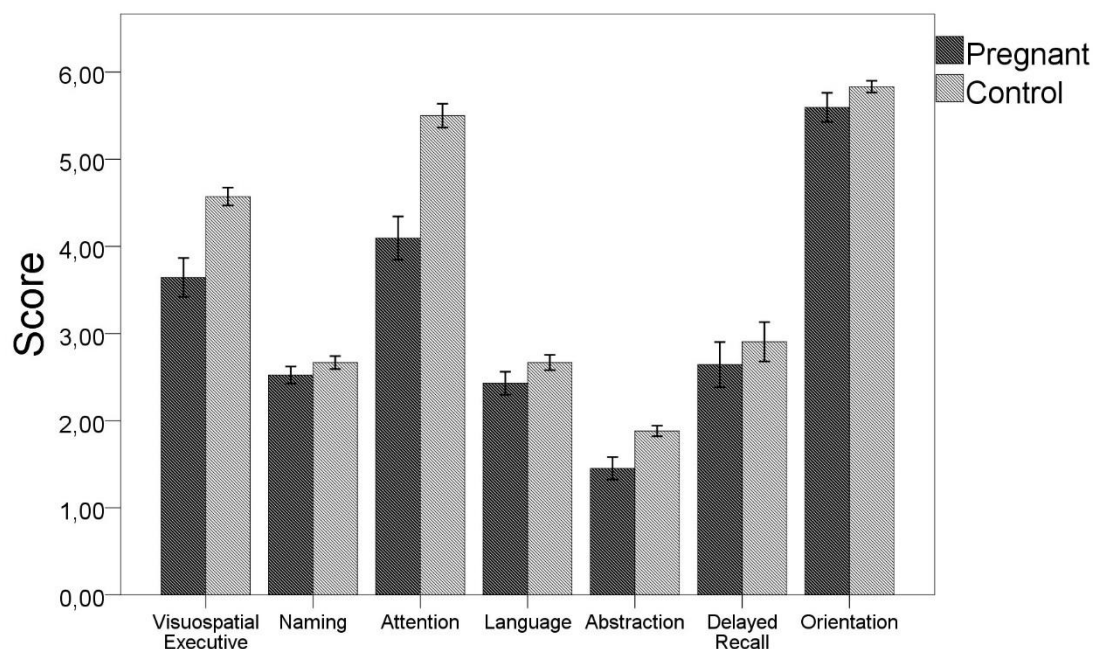


Figure 1. Comparison of Sub-parameters of Cognitive Assessment Level

The correlation between the cognitive assessment scores and the hormones in pregnant women are presented in Table 2. The relationship between the progesterone hormone levels and the scores obtained from the attention subdomain was found to be statistically significant ( $p = 0.030$ ). It is observed that the attention scores declined with increased progesterone levels during pregnancy. Similarly, the relationship between the progesterone hormone and the abstraction subdomain scores was found to be statistically significant ( $p = 0.025$ ).

Increased progesterone hormone levels were associated with reduced abstraction ability in pregnant women. In general, the relationship between the cognitive assessment score and the progesterone hormone was found to be statistically significant ( $p = 0.025$ ). High progesterone hormone levels in the pregnant women were associated with low levels of cognition. The effect of progesterone, age and TSH on cognitive assessment level is indicated in Figure 2.

Table 2. Correlation of Hormones and Cognitive Functions in Pregnant Women

	Progesterone		TSH		Ferritin	
	r	p	r	p	r	p
Visuospatial/Executive	-0.072	0.662	-0.070	0.662	0.055	0.736
Naming	-0.108	0.511	-0.079	0.619	0.307	0.054
Attention	-0.349	<b>0.030*</b>	-0.049	0.759	0.048	0.768
Language	-0.172	0.296	0.054	0.735	0.113	0.486
Abstraction	-0.358	<b>0.025*</b>	-0.085	0.592	0.020	0.903
Recall	-0.022	0.894	0.036	0.819	-0.003	0.984
Orientation	-0.241	0.139	0.085	0.592	0.051	0.757
Cognitive Assessment Score	-0.357	<b>0.025*</b>	-0.040	0.801	-0.050	0.761

Pearson Correlation test;  $\alpha:0,05$ ; \* Correlation is statistically significant

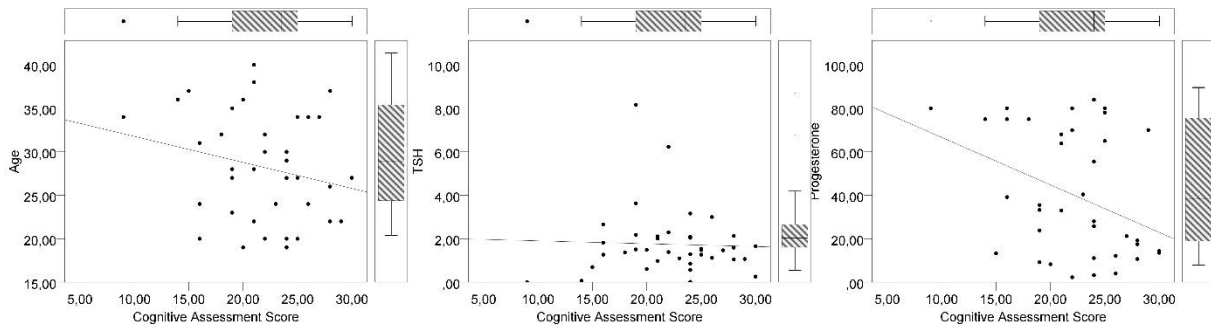


Figure 2. The effect of progesterone, age and TSH on cognitive assessment level

The effects of age; the levels of TSH, ferritin, and progesterone, and the gestational week on cognition were examined. The findings are presented in Table 3. Age; the levels of progesterone, TSH, ferritin, and the gestational week explained 52% of the change in cognition. Of these factors; the age of the pregnant woman, the levels of progesterone and TSH had a statistically significant effect on cognition ( $p = 0.033$ ;  $p = 0.04$ ;  $p = 0.001$ ,

respectively). Changes in the age and levels of progesterone and TSH will potentially act on the scores of cognitive assessment in pregnant women. Increased age and high progesterone and TSH levels cause a decline in cognitive assessment score. No significant effects of ferritin and TSH levels and the gestational week were observed to affect cognitive assessment score.

Table 3. Effect of Obstetric Characteristics on Cognitive Performance in Pregnant Women

	B	t	p
Age	-0.290	-0.17	0.033*
Progesterone	-0.039	-2.23	0.040*
Tsh	-0.901	-4.04	0.001*
Ferritin	-0.029	-1.98	0.057
Pregnancy Week	-0.073	-1.57	0.127

Robust Regression Analysis; Andrew M estimator;  $\alpha:0.05$ ;  $R^2:0.52$  \*Effect is statistically significant

Dependent Variables: Cognitive Assessment Score; Predictors: Age, Progesterone, Tsh, Ferritin, Pregnancy Week

### Discussion

Pregnancy is a physiologically critical stage of transformation for women. Besides the physical changes and the alterations in the endocrine system and hormone levels; several problems in mental and cognitive functions may arise in pregnancy. In our study, factors causing cognitive impairment in pregnancy were investigated besides comparing the cognitive levels between the pregnant and nonpregnant women. The

results demonstrated that visual execution, attention, and cognitive scores were lower in pregnant women compared to their nonpregnant counterparts. A study by De Groot et al. (2006) evaluated memory performance in pregnant women and in women in the control group (30). The authors reported that the memory performance was lower in pregnant women compared to the control group. In our study, recall function was found to be low in pregnant women. A study by Crawley, Grant, and Hinshaw (2008) compared the

severity of the cognitive decline in pregnancy compared to the control group (31). The comparison revealed that the cognitive scores of pregnant women were lower compared to those of women in the control group. The study by Aleshina et al. (2015) compared the cognitive scores between the groups of pregnant women suffering from autonomic nervous system disorders and the women in the control group (32). The authors observed significantly lower cognitive scores in pregnant women compared to the control group. Keskin et al. (2015) compared the cognitive functions between a group of pregnant women with gestational diabetes and a group of healthy pregnant women. Cognitive scores obtained from the assessment tests were significantly lower in pregnant women with gestational diabetes compared to the control group (33). The cognitive test scores of healthy pregnant women were reported to be  $23.7 \pm 3.7$ . It was observed that this value was close to the cognitive assessment scores ( $22.29 \pm 4.57$ ) of the pregnant women in our study. Several factors cause cognitive dysfunction during pregnancy. Of them, hormonal alterations are the leading factors. It was observed in the study that the hormones progesterone and TSH were significantly associated with the cognitive test scores. It was found out that as the progesterone and TSH levels increased, the cognitive test scores decreased. Gujski et al. (2017) carried out a study on thyroid hormones to determine cognitive impairment in postpartum women (34). That study demonstrated the effects of thyroid hormones on cognitive functions. In our study, the effect of TSH on cognitive functions in pregnant women was found out to be significant. High TSH levels are

associated with low scores in cognitive tests.

The number of studies conducted to determine the factors acting on the cognitive functions in pregnant women is quite a few in the literature. In our study, it was determined that not only progesterone and TSH hormones but also the age was effective on the cognitive functions during pregnancy. It was observed that increasing age in pregnant women was associated with cognitive impairment. Since cognitive impairment is usually observed in older people, several studies supporting this finding are available (35-37). High levels of progesterone and TSH have been observed as the major hormones affecting cognitive functions in pregnancy.

### **Conclusion**

Pregnancy is an important process in a woman's life. It has been observed that the cognitive alterations occurring in pregnancy are not permanent and they are associated with physiological changes and the age of the pregnant woman. The findings of our study provide important information to the literature due to the limited number of studies in this field. The study results are important as they will provide preventive measures to be taken for ensuring that pregnant women can spend this period in the most comfortable way as much as possible. Furthermore, it is important to identify the responsible factors causing cognitive changes and know that these change in cognitive functions in pregnant women will be transient. Our study results demonstrate that pregnant women do not only undergo physical changes, but they experience alterations in their mental and cognitive functions as well. Moreover, the results indicate that pregnant women should be supported throughout this period.

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### Conflict of Interest

The authors declare that they have no conflict of interest.

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