Stress reaction in pregnant women with various types of injuries

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ABSTRACT
The stress hormones cortisol and dehydroepiandrosterone were studied in 65 pregnant women admitted to the Karakalpak branch of the Republican Scientific Center for Emergency Medical Care over the past 3 years. The analysis of injuries showed that 20 women (30.7%) received an accident, 33 pregnant women (50.8%) – domestic injuries and 12 women (18.5%)- burns. According to the gestation period, 14 (21.5%) were injured in the first trimester, 29 (44.6%) in the second trimester and 22 (33.8%) pregnant women in the third trimester. There were 28 first-time pregnancies (43.1%), and 37 second-time pregnancies (56.9%). High cortisol levels were found in pregnant women with burns and accidents, which was 2.4 and 1.8 times higher compared to the normative data. According to the gestation period, the highest cortisol index was observed in pregnant women in the second trimester. Regardless of the gestation period in pregnant women with road accidents and burns, there was a significant 2-fold decrease in dehydroepiandrosterone compared with the normative data. In pregnant women with household injuries, the concentration of cortisol and dehydroepiandrosterone had no statistically significant differences from the normative data regardless of the gestation period.
Key words: pregnancy, stress reaction, trauma, complication.

INTRODUCTION

Injuries during pregnancy have increased dramatically over the past 25 years and are currently the number one cause of non-obstetric maternal mortality in the United States [1]. With extensive trauma, the risk of fetal death ranges from 40 to 50% [2]. Even with a minor injury, if it occurs during the first or second trimester, the probability of having a baby with prematurity or low birth weight increases [3]. Although this is rare in clinical settings, emergency physicians, trauma surgeons and obstetricians-gynecologists should know and be ready to treat various complications associated with trauma during pregnancy [4].

The sympathoadrenal system, which produces the hormones adrenaline and norepinephrine in response to stress, is another central component of the stress response. Unlike HGNO, which releases its effector hormones gradually, the release of catecholamines occurs as an immediate reaction to stress [5]. However, due to their hydrophilicity, catecholamines are not able to overcome the placental barrier in physiologically significant concentrations [6]. In addition, a huge number of catecholamines that enter the placenta are metabolized into inactive forms through the enzyme's monoamine oxidase and catechol-O-methyltransferase. Therefore, only a small amount of catecholamines can be transmitted from mother to fetus. But catecholamines can indirectly affect the metabolism of the fetus, changing the perfusion of the uterus and

placenta. A high level of maternal catecholamines circulating in the blood leads to a narrowing of placental blood vessels, a decrease in glucose intake into the fetal body and activation of catecholamine release in the fetus [7].

The hormonal status in physiological pregnancy has been studied quite well, there are a number of works considering hormonal indicators in the pathological course of pregnancy, but there are practically no studies considering the hormonal status of pregnant women with various injuries.

The aim of the study is to study the hormonal status of the sympathetic-adrenal system in pregnant women who have suffered various types of injuries.

MATERIALS AND METHODS

The study included 65 pregnant women aged 19 to 37 years who were admitted in an emergency to the Karakalpak branch of the Republican Scientific Center for Emergency Medical Care (for 2020-2022 According to the gestation period of the victims, pregnancy was from 7 to 39 weeks, while 14 (21.5%) were injured in the first trimester of pregnancy, 29 (44.6%) in the second trimester and 22 (33.8%) women in the third trimester. There were 28 (43.1%) first–time pregnancies, and 37 (56.9%) second-time pregnancies.

According to the nature of the injuries, the patients were divided into the following main 3 groups: group I - 20 pregnant women (30.7%) with road traffic injuries both in the form of a pedestrian, passenger and driver. Group II - 33 pregnant women (50.8%), with domestic injuries including falls. Group III – 12 pregnant women (18.5%), with various types of burns, both liquid and flame.

All pregnant women during the trauma during 1-2 days were assessed the hormonal status of the sympathetic-adrenal system such as cortisol and dehydroepiandrosterone in the blood serum. All hormonal studies were conducted in the laboratory of the private clinic «Grand Prime Medical» in the city of Nukus. Blood sampling was carried out in pregnant women on the first or second day after the injury. The study was carried out by the enzyme immunoassay method on an enzyme immunoassay analyzer of the company «MINDRAY MR-96A» (China), test kits of the company «ДС-ИФА» (Russia). The hormone concentration was determined automatically by the calibration curve and measured in nmol/L.

Statistical analysis: the results obtained were performed by conventional methods with the determination of the average value (M) and the average error of the arithmetic mean (m) using the Microsoft Excel computer program, with the calculation of the Student's t-test to compare the averages. Statistically significant differences were accepted at the significance level of $p<0.05$.

RESULTS AND DISCUSSION

An important place in assessing the adaptability of the maternal organism is a group of so-called «stress hormones», which include hormones of the adrenal cortex [8]. It should be noted that in pregnant women who received various injuries, regardless of the gestation period, the level of cortisol in the blood serum was significantly increased and exceeded the indicators of the normative group (Table 1).

Table 1. Cortisol indicators in pregnant women at the time of the injury

Cortisol nmol/l	Traffic accident n=20	Household n=33	Burns n=12	Standard data
<500	-	11 33,3±6,5	-	-
500-700	-	20 60,6±6,8	2 16,6±6,4	-
700-1000	18 90,0±3,5	2 6,0±3,3	5 41,6±9,9	-
More than 1000	2 10,0±3,5	-	5 41,6±9,7	-
average cortisol score	989,3±10,6*	560,4±14,2	1352,1±123,5*	548,2±12,3

Note: in the numerator abs. number, in the denominator - % content; where * is the reliability of differences in indicators compared to the group of women with physiological pregnancy (p≤0.001; C is the Mann-Whitney criterion)

It was found that a high level of cortisol corresponding to traumatic stress was found in 40 pregnant women, which is 61.5% of the total group. At the same time, cortisol levels of less than 500 nmol/l were detected in 8 cases (12.3%), mainly such hormone indicators were observed in women who had mild shock. It is noteworthy that the average cortisol values in the group with an accident at the time of the study amounted to 989.3±10.6 nmol/l and were significantly higher than the standards of 548.2±12.3 nmol/l (p≤ 0.001). The average cortisol values in the group with thermal burns were 1352.1±123.5 nmol/l at the time of the study. The lowest cortisol levels were found among women with domestic injuries, whose average was 560.4±14.2 nmol/l.

High cortisol levels at the time of injury, depending on the gestation period, indicate the reaction of the woman's body to the injury, characterized by a significant (p≤ 0.001) 2-fold excess of the standard index - 454.2 ± 29.3 nmol/l (Table 2).

Table 2. Indicators of cortisol in pregnant women, depending on the gestation period at the time of the injury

Cortisol nmol/l	type of injury			
	Traffic accident n=20	**Household n=33**	**Burns n=12**	**Standard**
1st trimester	n=6	n=7	n=1	n=14
	856,3±36,3*	557,8±61,7	967,5±29,4*	454,2±29,3
2nd trimester	n=8	n=13	n=8	n=29
	1103,7±38,6*	676,2±45,5	1097,2±47,3*	454,2±29,3
3rd trimester	n=6	n=13	n=3	n=22
	1167,8±41,3*	854,4±48,8	1133,4±26,9*	542,3±51,1

Note: * – reliability of differences in indicators compared with the group of women with physiological pregnancy (p≤0.001; C-Mann-Whitney criterion)

The highest indicator of the hormone was observed in the serum of women with a gestation period corresponding to the I and II trimester, and a clear dependence of the disorders on the type of trauma was revealed. Thus, an increase in cortisol concentration by 1.7-2.1 times occurred in road accidents - 856.3±36.3 in the first trimester and 1103.7±38.6 nmol/l, respectively, in the second trimester, with burns by 2.1 and 2.4 times or 967.5±29.4 and 1097.2±47.3 nmol/l, respectively. In case of household trauma, the indicators were also increased, but unreliably, but only 1.5 times 557.8 ±61.7 and 676.2±45.5 nmol/l, respectively. In the third trimester of pregnancy, a high level of cortisol was also established, regardless of the type of injury, significantly higher indicators were observed almost 2.1 times in pregnant women with road accidents and burns compared to the normative data, 1167.8±41.3 and 1133.4±26.9 nmol/l, respectively ($p \leq 0.005$). Thus, the first and second trimesters of pregnancy were the most vulnerable to stress.

The synthesis of estrogens in the fetoplacental system as a mandatory intermediate implies the formation of one of the androgens – dehydroepiandrosterone, capable of changing the balance of glucocorticoids and the content of which can be assessed during pregnancy and fetal condition [9]. To establish the effect of stress on the background of trauma on the course and outcome of pregnancy, we conducted a study of the content of dehydroepiandrosterone in blood serum, depending on the gestation period and the type of trauma suffered.

During the physiological course of pregnancy, the concentration of dehydroepiandrosterone has a wave-like character, with an increase in the second trimester and a decrease in the third by 1.5 times from the initial indicator - 2.09 ± 0.09, 2.25± 0.06 and 1.40± 0.03 mmol/l, respectively (Table 3).

Table 3. Indicators of dehydroepiandrosterone in pregnant women at the time of trauma and gestation

Dehydroepiandrosterone mmol/l				
	Traffic accident n=20	**Household n=33**	**Burns n=11**	**Standard**
1st trimester	n=6	n=7	n=1	n=14
	1,01±0,07*	1,97±0,03	0,97±0,3*	2,09±0,09
2nd trimester	n=8	n=13	n=8	n=29
	1,17±0,02*	2,01±0,02	1,13±0,05*	2,25±0,06
3rd trimester	n=6	n=13	n=3	n=22
	0,70±0,02*	1,27±0,03	0,84±0,01*	1,40±0,03

Note: * – reliability of differences in indicators compared with the group of women with physiological pregnancy ($p \leq 0.001$; C-Mann-Whitney criterion)

The results we obtained showed a significant decrease in the amount of dehydroepiandrosterone by almost 2 times in all women, regardless of the type of trauma and gestation period.

In the first trimester, the concentration of dehydroepiandrosterone in accidents and burns was reduced by 2 times compared with the normative data - to 1.01± 0.07 mmol/l, to 0.97±0.3 – respectively ($p \leq 0.001$). In pregnant women with injuries in the second trimester, the concentration of dehydroepiandrosterone was also significantly reduced in an accident, which was -1.17± 0.02 mmol/l, and in thermal trauma 1.13± 0.05 mmol/l ($p \leq 0.001$). In the third

trimester, the concentration of dehydroepiandrosterone on the background of trauma in pregnant women was also significantly reduced - to 0.70± 0.02 mmol/l in case of an accident and 0.84±0.01 mmol/l in case of burns, respectively ($p \leq 0.001$).

Only in the group with domestic injuries, the concentration of dehydroepiandrosterone had no statistically significant differences from the normative data, regardless of the gestation period. We believe that the reason for the decrease in dehydroepiandrosterone levels in women who suffered trauma was an increase in cortisol levels.

The ratio of dehydroepiandrosterone/cortisol characterizes the body's resistance to various disorders (stress, infection) [10]. In our case, during the physiological course of pregnancy, a decrease in this ratio was detected from 0.004± 0.0008 in the first trimester to 0.001± 0.00001, respectively, in the third (Table 4).

Table 4. The ratio of dehydroepiandrosterone / cortisol in pregnant women at the time of trauma and gestation

DEAS/ Cortisol	Types of injuries			
	Traffic accident n=20	**Household n=33**	**thermal n=11**	**Standard**
1st trimester	n=6	n=7	n=1	n=14
	0,001±0,0002*	0,001±0,0001*	0,001±0,0002*	0,004±0,0008
2nd trimester	n=8	n=13	n=8	n=29
	0,001±0,0002*	0,001±0,0002*	0,001±0,0002*	0,004±0,0003
3rd trimester	n=6	n=13	n=3	n=22
	0,0005±0,0001*	0,0006±0,0001*	0,0007±0,0002*	0,001±0,00001

Note: * – reliability of differences in indicators compared with the group of women with physiological pregnancy ($p \leq 0.001$; C-Mann-Whitney criterion)

This indicates that a high level of cortisol at the end of gestation is necessary to meet the increased metabolic needs of the pregnant woman's body by activating carbohydrate synthesis and lipolysis. Cortisol controls the transport of glucose through the placenta. In addition, the hormone is important for the formation of enzyme systems of the liver, the epithelium of the small intestine, fetal lung cells: the development of the alveolar epithelium and the secretion of surfactant, which contribute to the expansion of the lungs at the first breath [8].

In women who suffered trauma, this ratio was reduced by 4 times in the first and second trimester, and in the third – by 1.6-2 times compared with the indicators of women with a physiological course of pregnancy ($p \leq 0.001$). Such a situation creates a great danger for pregnancy, since a decrease in stability in the ratio of hormones entails the development of a high risk of termination of pregnancy.

The discrepancy between the level of a number of studied indicators in pregnant women who have suffered trauma, the norms of healthy women with the physiological course of pregnancy, in some cases is not a sign of pathology, but only indicates adaptive changes in the body of pregnant women under the influence of trauma.

The results, indicating a violation of the intensity of transformations of the studied steroid precursors, allow us to conclude that these stages can change under the influence of trauma and stress, namely, a direct increase in cortisol during gestation, thereby representing "vulnerable

points" of the risk of termination of pregnancy and the development of infectious (septic) processes in pregnant women with injuries.

CONCLUSION

1. Cortisol indices in pregnant women with burns amounted to 1352.1±123.5 nmol/l, which was 2.4 times higher compared to the normative data, also high cortisol indices were noted in pregnant women with road accidents, which amounted to 989.3±10.6 nmol/l and were significantly higher 1.8 times compared to the standards of 548.2±12.3 nmol/ll ($p \leq 0.001$).
2. According to the gestation period, the highest cortisol index was observed in the serum of pregnant women in the second trimester. The lowest and unreliable indicators of cortisol were found among pregnant women with domestic injuries.
3. Regardless of the gestation period in pregnant women with road accidents and burns, there was a significant 2-fold decrease in dehydroepiandrosterone compared with the normative data. In pregnant women with household injuries, the concentration of dehydroepiandrosterone had no statistically significant differences from the normative data, regardless of the gestation period. The reason for the decrease in the level of dehydroepiandrosterone in women who had an injury was an increase in cortisol levels.
4. In pregnant women who have suffered trauma, the ratio of dehydroepiandrosterone/Cortisol was significantly reduced by 4 times in the first and second trimester, while in the third trimester this indicator was reduced by 1.6-2 times compared with the indicators of normative data.

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