

## THE INFLUENCE OF PRENATAL STRESS ON DELIVERY OUTCOME

*Dragan Krstić<sup>1</sup>, Sonja Pop-Trajković<sup>2</sup>, Ljiljana Mirković<sup>3</sup>, Darko Marinković<sup>4</sup>, Jelena Krstić<sup>5</sup>*

<sup>1</sup>General Hospital Leskovac, Department of Gynecology with Perinatology, Serbia

<sup>2</sup>Clinical Center Niš, Clinic of Gynecology with Obstetrics, Serbia

<sup>3</sup>Clinical Center of Serbia, Belgrade, Institute of Gynecology with Obstetrics, Serbia

<sup>4</sup>General Hospital Uzice, Department of Gynecology with Obstetrics, Serbia

<sup>5</sup>General Hospital Leskovac, Department of Medical Biochemistry, Serbia

E-mail: adela@ptt.yu

**Summary.** *The aim of the paper is to prove a birth adaptation to the quality of life of a pregnant woman by the influence of prenatal stress on variability of biological pregnancy duration. We investigated: the incidence of cesarean section (SC), findings on admission in women with previous SC and duration of gravidic amenorrhea before, during and after the bombardment, as well as the low quality of life during which pregnant women were exposed to stress. The data were collected retrospectively from disease histories in Obstetric Department of the General Hospital in Leskovac. This hospital has the only Maternity Ward to which 250.000 inhabitants of the Jablanica District at the South of Serbia gravitate, in which about 2300 births are registered out per year. The study included 1448 births in the period from March 24 – June 9, 1999, the year before, and one year after the NATO aggression against the FR of Yugoslavia. The data were statistically processed by the  $\chi^2$  and Kolgomorov-Smirnov tests and graphically presented by Microsoft Excel Program. The incidence of SC significantly decreased, while the incidence of vaginal births after previous SC increased during the period of bombardment compared to the same period in the previous and the next year. The finding on admission in pregnant women with previous SC and time of birth compared to the due date of delivery point to an earlier spontaneous birth beginning (biologically shorter pregnancy duration) as the cause this phenomenon. The mechanism of prenatal stress shortens the biological pregnancy duration and, therewith, makes the delivery of a pregnant woman with low life quality quicker, easier and more safe with fewer indications for SC.*

**Key words:** *Pregnancy, cesarean section, war, stress, adaptation*

### Introduction

The practice of doing cesarean section (SC) exclusively because of a patient's will has reached broad popularity in the majority of developed countries in the world. The fear of vaginal birth and opinion that it causes such harm to an organism that it diminishes the life quality of a pregnant woman just gives these women right to choose SC (1).

However, we are all witnesses that with better social treatment of pregnant women, and generally their better life quality, the incidence of SC, apart from the previous attitude, increases in all societies with better quality of life.

In the Leskovac Maternity Ward, where we still insist on natural birth (even in spite of a pregnant woman's will) the incidence of SC has significantly increased in the past two decades and still continues to grow. Despite fear and negative feelings towards SC, now for the first time it has become statistically significant even in Gypsy population. At the same time, the percentage of 13 and 14-year-old primiparas has increased, which is "in prediction of bad life outcome". Therefore, the quality of life in Gypsy communities is still far below average, which also goes for CS (2).

The life quality is a complex term which is very hard to quantify since, besides economic standards, depends on other hardly measurable factors. The association with the influence on delivery can be proved only by comparing events generally accepted as tragic ones, such was the bombardment of the FR of Yugoslavia. The bombardment of the whole territory from March 24 – June 9, 1999 was described as "the war against the health of one nation" and is characterized by intimidating the nation and polluting the environment (3).

At that time, the life quality of pregnant women corresponded to a very low quality of life, which is characterized by greater exposure to stress. Since the perinatal protection was normally functioning, there was an opportunity to investigate the effects of the so-called "prenatal stress" exclusively as the consequence of fear and social and biological uncertainty.

Prenatal stress denotes changes in the levels of adrenalin, plasma epinephrine and hydrocorticosteroids followed by hyperventilation, tachycardia and many other upsetting effects registered during pregnancy, both in the mother exposed to stress and fetus. The influence of unpleasant emotions that the mother under stress transmits to the fetus through hormones has been inves-

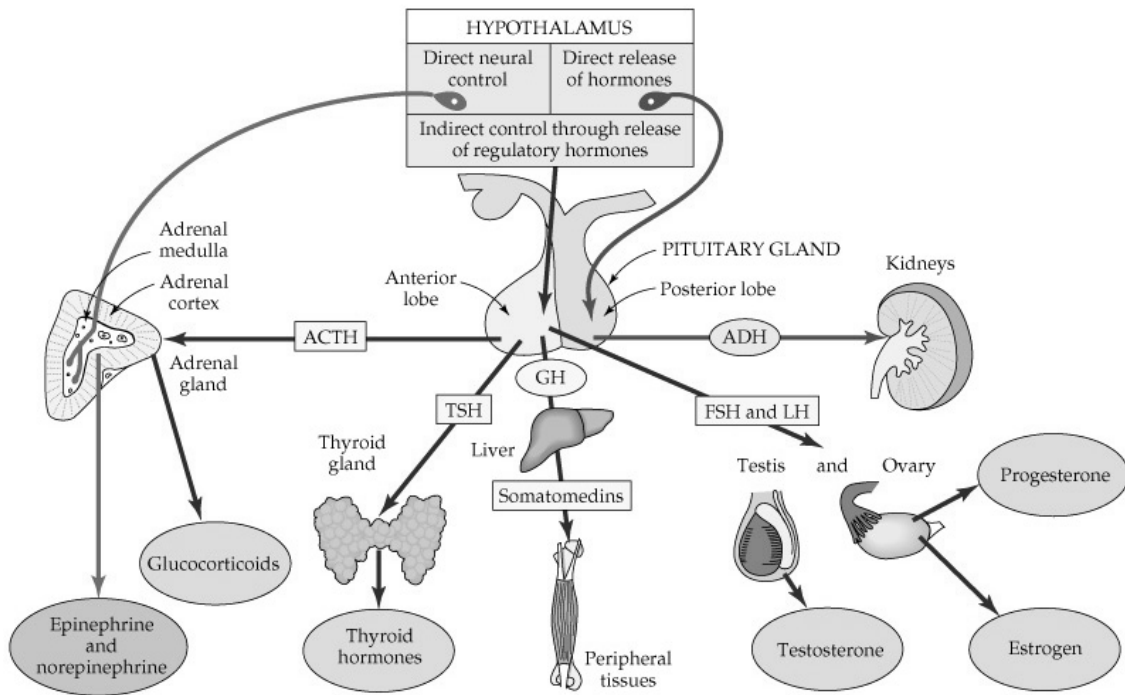


Fig. 1. Hypothalamic-pituitary-adrenocortical axis and sympathetic-adrenomedullary system in the neuroendocrine control of an organism (taken from the lecture of Prof. Dr. V.Djordjevic)

tigated in experiments on animals, in pregnant women during wars, in those suffering because of poverty and racial/ethnic segregation. However, Freud described normal birth as our "first experience of anxiety", recognizing at the end of his life that fetal memory exists, and stress before birth is an integral part of life experience influencing thus the formation of one's personality (4).

As the term "stress" is widely used and includes many terms, misunderstandings of its causes and consequences are very frequent. Under stress, the activities of hypothalamic-pituitary-adrenocortical (HPA) axis and sympathetic-adreno-medullary (SAM) system are increased. The observations of many authors point to their influence on nearly all hormones, while the influence of stress on the concentration of thyroxin and insulin is less marked (Figure 1). Precisely, stress is "the sum of different stimuli that damage or do harm to the organism and which can stimulate the excretion of adrenocorticotrophic hormone (ACTH). Different kinds of stressors can provoke an increased ACTH secretion, thus dividing it into systemic and neurogenic. However, regardless of the fact whether it is physical, biological or psychological trauma, in the further course, the reaction of endocrine system is the same (5).

Its influence in pregnancy is associated with increased release of cortico-releasing hormone (CRH) in placenta. This increase is registered in pregnant women under stress before normal increase which occurs within a due date, especially in the last trimester, which is to a certain extent a part of normally increased basal metabolism of a pregnant woman. But, as pregnancy does not significantly influence laboratory analyses, one can

conclude that pregnant women are generally less sensitive to stress (6).

The exposure of an organism to stressful environment factors may have in certain cases a positive effect, but also, it can decrease the ability of the organism to maintain homeostasis. After each more severe trauma, psychic or physical, there is a manifestation of the syndrome comprising shock, resistance and exhaustion, that is hypothermia, hypotonia, hypochloremia and hypoglycemia, and after several days, the excretion of 17-Ks and aldosterone increases. Though the reaction is mild, similar changes of laboratory analyses point to metabolic changes occurring under the influence of stress, which can be of great importance for the development of fetus. A higher level of free CRH of placental origin has been proved in the fetal circulation with probably the same influence on its metabolism (7).

These metabolic changes, blood circulation centralization and oxidative disbalance in pregnant women being under stress are followed by cytokines and prostaglandins E2 and F2α from decidua which, acutely, can bring about a miscarriage or preterm birth. Chronically, the prenatal stress is proved to be associated with lower birth weight and slower growth rate after birth (8).

There are many studies investigating laboratory analyses in reactions of pregnant women to stress. In those experiments, the tests created to cause pain or discomfort, cognitive or psychological stress were used in order to assess the changes in the blood pressure, heart rate and/or the cortisol level as the measure of stress reaction. From the results of these studies, we can draw the conclusion that physiological reactions to

stress during pregnancy are milder. Their defects are methodological limitations which appear when reactions of different groups of people are investigated (9).

The reaction to stress differs among groups and individuals, since the reaction pattern is individually programmed in the intrauterine development. A certain pattern of behavior is programmed and transmitted transgenerationally by non-genomically different activities of SAM system and HPA axis. This activity is typical of the life quality and behavior in a certain social milieu (10).

It has been proved that the intrauterine development of rats that have been exposed to stress prenatally modulates the pattern of excessive response to stressful situations in adulthood. An excessive reaction even to minor stress may lead to the clinical state of shock, resistance and exhaustion. In the group whose intrauterine development was not under the influence of prenatal stress, the reaction to the same level of stress was milder and with fewer consequences (11).

More significant production of CRH by placenta has been proved in all primates. However, future investigations should allow for specifics of the mechanisms that regulate this influence with regard to the species. There is still no evidence of the mechanisms of stress that affect the ontologic development of the HPA axis in humans. Today, there are more and more researches investigating the interactions of fetal, maternal and placental hormones (12).

Placental production and CRH release comprise both maternal and fetal components which are cortisol-controlled by both sides. It has been proved that cortisol, along with other hormones and opiates which are intensively secreted under stress, passes through the placental barrier. This possibility has at least two consequences for a pregnant woman: (1) the influence on the birth, (2) desensitization of hypophysial corticotropes and further, "protection" of pregnant women from stress (that is the release of ACTH and beta endorphine). There are indications that beta E influences fetal learning, and possibly the nervous system development (13).

The main circulating glucocorticoids – cortisol and hydrocortisol are synthesized directly under the influence of ACTH in zona fasciculata in the suprarenal cortex.

These are pleotropic hormones characterized by anti-inflammatory and immunosuppressive characteristics just as their synthetic analogues which are therefore used in the therapy of different imbalances. In the case of an overdose, there are numerous side effects such as the symptoms of cardiovascular diseases, osteoporosis, miopathy, diabetes mellitus, depression, immunosuppression. The causes are: the hyperproduction of free oxygen radicals (ROS), peroxynitrites ONOO and disorders of tetrahydrobiopterin (BH4), that is inducing of the cellular oxidative stress. Free radicals of the cell initiate apoptosis or oxidative modification of proteins. In people constantly exposed to stress, these mechanisms accelerate the process of aging. The covalent modification of proteins which is caused or induced by free radicals' reactive intermediates or their final products has been a proved substrate of the preterm aging

syndromes (Hutchinson-Guilford, Verner's syndrome). Therefore, the adaptation to stress, besides the balance of neurotransmitters in the brain and hormones in the circulation, presupposes the maintaining of balance between anti-oxidants and the cell free radicals (14).

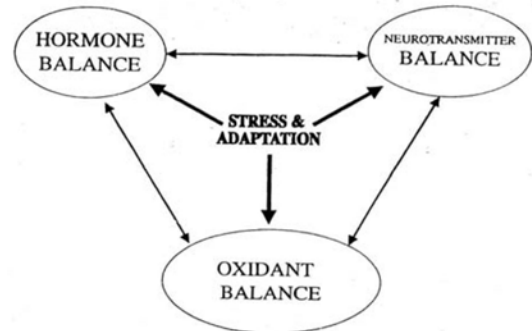


Fig. 2. Adaptable mechanisms during stress (taken from the lecture of Prof. Dr. V. Djordjevic)

The concept of the common adaptation syndrome means that the organism has genetically determined quantity of adaptable energy which progressively decreases in every exposure to stress. The alostatic damages of the body, which naturally occur during the process of aging as the consequence of stress accumulation, is particularly characterized by the groups with transgenerational pattern of excessive reaction to provocative situations (15).

Similar consequences of stress accumulation may also be seen in fetus. The influence of stress hormones on the lungs' maturity and simultaneous decreasing of the grey mass of cerebral cortex suggest the negative influence of prenatal stress on the CNS development, which can be seen in prematurely born children under the corticosteroid therapy (16).

As for the influence of stress on other functions of fetus, there is a hypothesis which can be used in the assessment of the kind of delivery. According to this theory, the effects of prenatal stress are not always pathological (non-adaptable explanation). On the contrary, a mother can adopt themselves and fetuses in some functional way to birth and life even under hard conditions (adaptable explanation) (17).

## Aims

With this clinical study presenting births one year before, during and after the bombardment of the FR of Yugoslavia, we want to prove the following working hypothesis: in the last trimester of pregnancy, stress shortens its biological duration, by which it adapts birth to bad conditions of the outside world, so that it becomes more safe, with fewer indications for CS.

## Methodology and selection of patients

Such influence of stress will be proved by retrospective study investigating the incidence of CS, VBAC

(vaginal birth after cesarean), and post-date births in the same intervals before, during and one year after the NATO aggression in 1999. The influence of stress on duration of pregnancy will be additionally considered by analyzing the admission finding, duration and kind of birth after previous CS compared to the due date.

The data on 1448 births registered between March 24 and June 9, 1998, 1999 and 2000 were compared. In statistic evaluation of the VBAC incidence, Kolmogorov-Smirnov test was used. In the assessment of statistically significant difference in the incidence of CS, we used the  $\chi^2$  test, since this manifestation was more frequent. The results were presented graphically by Microsoft Excel Programme.

The data were obtained from the Service of Gynecology and Perinatology of Regional Hospital in Leskovac. This hospital has the only Maternity Ward to which 250.000 inhabitants of the Jablanica District at the South of Serbia gravitate, in which about 2300 births are registered per year.

**Results**

There is a significant difference in the number of CS in regard to the period from March 24 to June 9, 1998, 1999 and 2000 and the sum of all three years. (Table 1 and Figure 3).

Table 1. Kind of birth in the examined groups before, during and after the bombardment in 1999

Time interval	March 24 – June 9 1998	March 24 – June 9 1999	March 24 – June 9 2000
Total CS	83 14.85%	37 8.56%	77 16.85%
Repeated CS	31 5.55%	15 3.47%	23 5.03%
VBAC	2 0.36%	8 1.85%	1 0.22%
Vacuum (V)	17 3.04%	28 6.48%	13 2.84%
Others	426 76.30%	344 79.63%	343 75.05%
Total	559 100.00%	432 100.00%	457 100.00%

There is no significant difference between 1998 and 2000 in the period examined. The number of births ended by CS is statistically significantly smaller during the bombardment compared to the year before and after.

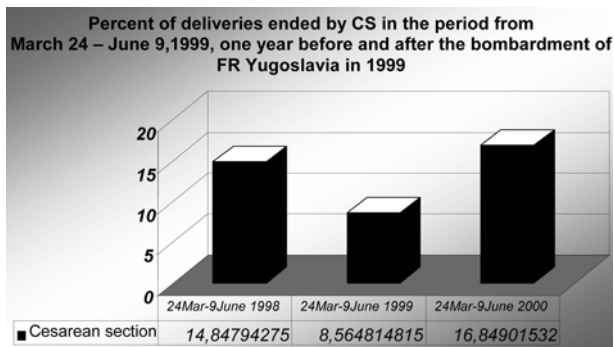


Fig. 3. Cesarean section before, during and after the bombardment of FR Yugoslavia in 1999

By analyzing the statistically significant difference in the number of VBAC in these periods (Table 1 and Figure 4) by Kolgomorov-Smirnov test, it can be concluded that there is a great percentual difference – its statistical significance is limiting (p=0.05).

In making approximations for the period of bombardment, the test shows an increase up to the level of significance when compared to the same period one year after.

Therefore, there is a clear indication that this manifestation would be more statistically significant if applied on a greater number of cases when compared to the same period one year before.

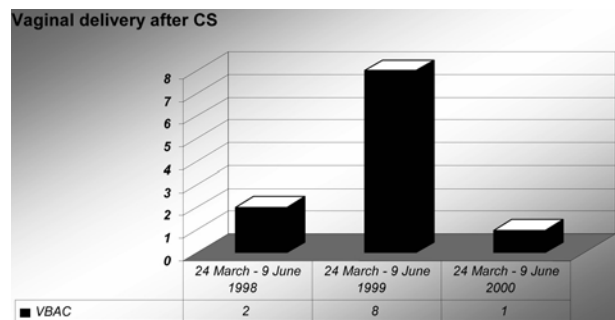


Fig. 4. The incidence of VBAC before, during and after the bombardment of the FR of Yugoslavia in 1999

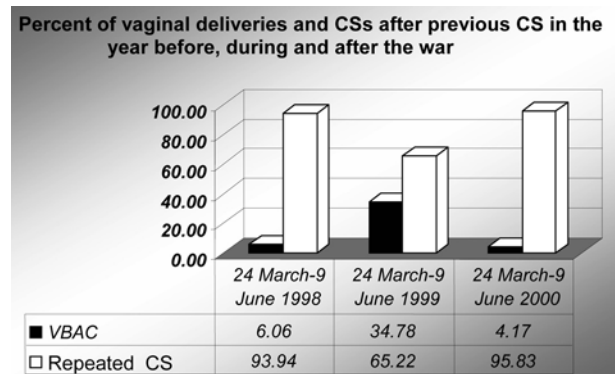


Fig. 5. Births after previous CS before, during and after the bombardment of the FR of Yugoslavia in 1999

The number of births in pregnant women who previously had CS is the same in all three groups and differs only in the frequency of repeated CSs. In the period of bombardment, the number vaginal births was greater, since they started more than one week before the due date (Table 2.). The finding on admission always pointed to the advanced phase and such decision did not put pregnant women at greater risk, while repeated CS was planned and done in the last week of gravidic amonorrhoea on the due date or after it, with the Bishop score under seven (Table 3).

Table 2. Analysis of vaginal births during the bombardment after previous CS

Number	Amenorrhea	Cervix	Dilatation	Delivery	Appgar
1	-38	Flat	3.0 cm	5 <sup>h</sup>	10
2	-17	Flat	4.5 cm	3 <sup>h</sup>	9
3	-13	Flat	1.5 cm	5 <sup>h</sup> 15 <sub>min</sub>	10
4	-12	Flat	4.5 cm	7 <sup>h</sup> 30 <sub>min</sub>	9
5	-11	Flat	3.0 cm	4 <sup>h</sup>	10
6	-11	Flat	7.5 cm	1 <sup>h</sup> 45 <sub>min</sub>	10
7	-8	Flat	6.0 cm	4 <sup>h</sup> 45 <sub>min</sub>	10
8	-3	Flat	4.5 cm	5 <sup>h</sup>	9

Table 3. Analysis of repeated CS in the period from March 24 – June 9, 1999

Repeated CS	Amenorrhea	Bishop	Hospitalization	Appgar
1	-6	<7	8 days	10
2	-2	<7	4 days	10
3	-5	<7	5 days	10
4	-12	>7	7 days	10
5	-14	>7	8 days	10
6	-6	<7	7 days	10
7	-6	<7	5 days	8
8	-7	<7	4 days	10
9	On date	<7	7 days	10
10	On date	<7	5 days	10
11	On date	<7	7 days	10
12	+4	<7	7 days	10
13	+2	<7	5 days	5
14	+1	<7	5 days	10
15	+5	<7	11 days	10

By the analysis of significant difference in the number of postdate deliveries in the period from March 24 – June 9, 1998, 1999 and 2000 (Table 4) and the sum of all three years by using the  $\chi^2$  test, we determined a statistically significant difference. By comparing the same period of the pre-war 1998 and post-war 2000, we did not find any statistically significant difference. Therefore, the postdate deliveries were statistically significantly less frequent in the period of bombardment (Figure 6).

Table 4. Date of birth compared to the expected duration of gravidary amenorrhea

Total number of deliveries	March 24 - June 9 1998		March 24 - June 9 1999		March 24 - June 9 2000	
	N = 559		N = 432		N = 457	
Before due date	308	55.10%	273	63.19%	252	55.14%
On due date	27	4.83%	31	7.18%	23	5.03%
After due date	184	32.92%	93	21.53%	160	35.01%
Unknown date	40	7.16%	35	8.10%	22	4.81%

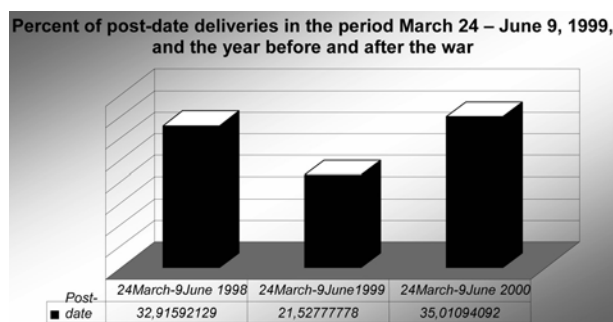


Fig. 6. Duration of pregnancy before, during and after the bombardment in 1999

### Comments on results

The influence of stress on delivery during the three-month-long bombardment is presented in Table 1. The overall number of artificial births decreased due to an obviously smaller number of CSs (Figure 3). The number of vacuum extractions in the period of bombardment compared to the same period in 1998 and 2000 parallelly increased with VBAC (in such births, our protocol requires the use of vacuum in order to relax the uterine muscle in expulsion). From negligible number of cases at the beginning, VBAC became statistically significant (Figure 4), while the number of repeated CSs decreased in the period of bombardment (Figure 5).

The increased percentage of VBAC was explained by comparative analysis of these births and repeated CSs in the period from March 24 – June 9, 1999 (Table 2, Table 3). With the exception in one case, all VBAC were done more than one week before the due date. The finding on admission confirms medical indications when the way of ending birth is concerned. These pregnant women came into hospital with flat cervix and great dilatation, which pointed to the advanced phase of pregnancy. That we did not insist on vaginal birth without reasons, confirms its short duration without uterotonics with satisfactory Appgar score. Repeated CS was elective and done in the last week on the expected date or after it with the Bishop score under 7. Twice, we had the cases of births when we suspected of some disproportion.

The ratio between expected duration of gravidic amenorrhea and actual pregnancy duration is the same before and after the bombardment. The literature data show that they overlap in only 5% of cases. The outside conditions were equal in these cases and accidental influences as the possible causes of difference between these two variables were annulled. However, the percentage of women who had deliveries after the due date significantly decreased during the bombardment (Table 4). As the course of pregnancy in all examinees up to the third trimester was before the bombardment and all other conditions were the same, a new ratio between pre- and post-date deliveries during the bombardment shows that real, biological duration of pregnancy was shorter in the last trimester under the influence of stress (Figure 6).

## Discussion

With regard to duration of bombardment of civilians and its sudden cause of stress of great intensity, under the same conditions of perinatal protection, we had an opportunity to prove the influence of stress on the CS incidence by comparing it with the same periods one year before and after the bombardment.

An obviously lower percentage of CS as well as a greater number of vacuums and VBAC during the bombardment was falsely interpreted as the need of the hospital to economize on surgical material. There were some attitudes that the war time in the FR of Yugoslavia reduced CS to an earlier "real" percentage of cesareans by compelling doctors to consider these indications more seriously.

However, the analysis presented in the comments on results confirms our hypothesis that the cause was an earlier delivery. The lower incidence of CS is statistically significantly associated with earlier beginning of delivery during the bombardment. This is possible only if there is an influence of prenatal stress on a pregnant woman and intrauterine fetus development. Besides stress affecting pregnant woman, all other influences of the war time (including stress of the staff, attitude of the management and hospital conditions) could not be the cause of an earlier beginning of birth after biologically shorter duration of pregnancy in women living under unfavorable conditions.

Even though the influence of prenatal stress on intrauterine development is recognized today and its mechanisms are partly explained, there is not enough clinical evidence that the adapting of pregnancy to stress during war brings about the consequences in the course of birth, neonatal and adult period.

Based on previous knowledge, a greater number of spontaneous miscarriages and preterm birth is expected (18).

Stress has its own postponed effects that could be manifested after the war as post-traumatic stress disorder (PTSD). Within this syndrome in pregnant women, besides miscarriages and earlier deaths of fetuses, smaller body mass of a newborn with delayed growing rate was also proved (19).

After the Gulf War, there were only reports on increased incidence of spontaneous miscarriages which were supposed to be within the PTSD symptoms and/or pollution of the environment (20).

In Israel, the influence of intrauterine stress on the incidence of schizophrenia in children whose mothers suffered the stress during bombardment was investigated, and there was no proof of its increase (21).

Furthermore, in Israel, an increase of prematurity as the consequence of fear in pregnant women exposed to bombardment has not been proved during the Gulf War (22).

After the terrorist attack on New York on September 11, the Americans did not manage to prove the influence of stress on pregnancy duration (23).

However, analyzing the level of cortisol in saliva, the PTSD in babies whose mothers were exposed to the attack on the World Trade Center has been proved (24).

Some papers of the authors from former republics of the Socialist Federative Republic of Yugoslavia report the changes in the perinatal outcome and number of births in certain regions, but, only after the war and probably as a result of emigrations (25).

Therefore, in the last ten years of waging wars in our country and the whole world, there are some indications that prenatal stress affects development and course of pregnancy, but there is no evidence of increased incidence of premature births. In all these examples, this fact might be the consequence of the evacuation of pregnant women from the war zone, short duration of conflicts or inability to react properly during war clashes.

However, an increased rate of prematurity has not been verified in our country where the bombardment of the whole territory lasted three months without any possibility to evacuate the population into safety zones and where the health care protection of the population was properly functioning all the time. A good perinatal outcome, which is always the consequence of low prematurity rate, shows that the shorter pregnancy duration during the bombardment is associated with accelerated maturation of fetus under the stress (26).

The analysis of births after the previous CS confirms that the kind of birth is closely associated with discrepancy between the expected and real duration of pregnancy. Although never recognized as an official attitude, "once CS, always CS" is confirmed in the practice whenever pregnancy reaches or exceeds the due date. VBAC practically occurs only when a birth starts suddenly surprising both a pregnant woman and doctors or when on admission into hospital we register an advanced phase of birth. Therefore, their statistically significant occurrence during the bombardment supports the hypothesis that the intrauterine development can be of different duration and depends upon the quality of a mother's life.

It is logical that accelerated intrauterine fetus development under stress, besides an earlier birth, is characterized by lower body mass at birth. Though not being associated with shorter pregnancy duration, several studies have pointed to a smaller body mass with chronic prenatal stress. A natural consequence of bearing a newborn with lower body weight completely ready for the extrauterine life is an easier birth with fewer indications for CS both in a mother and fetus. Then, the vaginal birth carries less risk of injuries which are the cause of so much fear in pregnant women, and the possibility of negative influence on the life quality is also decreased. Therefore, a lower SC incidence during a war stands for the adaptation of the pregnant woman to bad outside conditions (preparation for "escape or conflict") that require quick recovery after giving birth.

Allostatic damages of an adult organism in the process of aging are analogous to the influence of stress on a shorter intrauterine development. Duration of pregnancy, delivery, life span and death are variables depending on genetic predisposition and exposure to stress.

## Conclusion

The mechanisms of prenatal stress significantly decrease the SC incidence with earlier beginning of birth after biologically shorter duration of pregnancy in

women living under unfavorable conditions. A higher incidence of CS is the consequence of greater body mass of a newborn due to longer pregnancy duration under less stressful and more quality life.

## References

1. Grbović-Sekulić S. Caesarean section use. *J Gynecol Perinatal* 2005; 38(1): 3–4.
2. Krstić D., Popović M., Milenković S. Ljubić B. The adolescents deliver and demographic implication. 13th Congress UGOJ Belgrade 2001; Congress book, pp. 272–275.
3. Ashford MW, Gottstein U. The impact on civilians of the bombing of Kosovo and Serbia. *Med Confl Surviv* 2000; 16(3): 267–80.
4. Lloyd deMause. Restaging prenatal and birth traumas in war and social violence. *J Psychohistory* 1995; 23(4): 344–392.
5. Đurić D, Nešović M. Stress and function of neuroendocrine system. In: Đurić D. (ed), *Basics of neuroendocrine system*. ZUNS, Belgrade, 1985: 502–11.
6. Krstić J. Biochemical parameters in pregnancy. Specialization work. Institute of Medical Biochemistry, Faculty of medicine, University of Nis, 2001.
7. Miladinović Segedi Lj, Milašinović Lj. Metabolism. In: Milašinović Lj. (ed), *Clinical physiology in pregnancy*. IPSKK Kosmos, Beograd, 2005. p. 246–57.
8. Rich-Edwards JW, Grizzard TA. Psychosocial stress and neuroendocrine mechanisms in preterm delivery. *Am J Obstet Gynecol* 2005; 192(5 Suppl): S30–5.
9. de Weerth C, Buitelaar JK. Physiological stress reactivity in human pregnancy - a review. *Neurosci Biobehav Rev* 2005; 29(2): 295–312.
10. Champagne F, Meaney MJ. Like mother, like daughter: evidence for non-genomic transmission of parental behavior and stress responsivity. *Prog Brain Res* 2001; 133: 287–302.
11. Neumann ID, Kromer SA, Bosch OJ. Effects of psycho-social stress during pregnancy on neuroendocrine and behavioural parameters in lactation depend on the genetically determined stress vulnerability. *Psychoneuroendocrinology* 2005; 30(8): 791–806.
12. Lockwood CJ, Radunovic N, Nastic D, Petkovic S, Aigner S, Berkowitz GS. Corticotropin-releasing hormone and related pituitary-adrenal axis hormones in fetal and maternal blood during the second half of pregnancy. *J Psychosom Res* 2002; 53(4): 865–71.
13. Sandman CA, Wadhwa P, Glynn L, Chisz-Demet A, Porto M, Garite TJ. Corticotrophin-releasing hormone and fetal responses in human pregnancy. *Ann N Y Acad Sci* 1999; 897: 66–75.
14. Vidosava BĐ, Dušica DP. Biochemistry markers of oxidative stress in experimental and clinical medicine. Congress book. Institute of biochemistry, Faculty of medicine, University of Nis, 2006.
15. Seckl JR. Prenatal glucocorticoids and long-term programming. *Eur J Endocrinol* 2004; 151 (3): U49–62.
16. Murphy BP, Inder TE, Huppi PS, Warfield S, Zientara GP, Kikinis R. Impaired cerebral cortical gray matter growth after treatment with dexamethasone for neonatal chronic lung disease. *Pediatrics* 2001; 107(2): 217–21.
17. Kaiser S, Sachser N. The effects of prenatal social stress on behaviour: mechanisms and function. *Neurosci Biobehav Rev* 2005; 29(2): 283–94.
18. Araneta MR, Kamens DR, Zau AC, Gastanaga VM, Schlangen KM, Hiliopoulos KM. Conception and pregnancy during the Persian Gulf War: the risk to women veterans. *Ann Epidemiol* 2004; 14(2): 109–16.
19. Waddington A, Ampelas JF, Mauriac F, Bronchard M, Zeltner L, Mallat V. Post-traumatic stress disorder (PTSD): the syndrome with multiple faces *Encephale* 2003; 29(1): 20–7.
20. Rajab KE, Mohammad AM, Mustafa F. Incidence of spontaneous abortion in Bahrain before and after the Gulf War of 1991. *Volume 68, Issue 2, 2000: 139–144*.
21. Seltzer JP, Cantor-Graae E, Nahon D, Levav I, Aleman A, Kahn RS. No relationship between risk of schizophrenia and prenatal exposure to stress during the Six-Day War or Yom Kippur War in Israel. *Schizophr Res* 2003; 63(1-2): 131–5.
22. Schenker E, Mor-Yosef S. Did anxiety during the Gulf War cause premature delivery? *Psychol Rep* 1993; 72(2): 600–2.
23. Rich-Edwards JW, Kleinman KP, Strong EF, Oken E, Gillman MW. Preterm delivery in Boston before and after September 11<sup>th</sup>, 2001. *Epidemiology* 2005; 16(3): 323–7.
24. Yehuda R, Mulherin Engel S, Brand SR, Seckl J, Marcus SM, Berkowitz GS. Transgenerational effects of posttraumatic stress disorder in babies of mothers exposed to the World Trade Center attacks during pregnancy. *J Clin Endocrinol Metab* 2005 90(7): 4115–4118; as doi:10.1210/jc.2005-0550.
25. Begic K, Dizdarevic J, Boloban H, Hadic N, Maksic H. Perinatal mortality at the Gynecology-Obstetrical Clinic of the Clinical Center in Sarajevo in 2001 *Med Arh*, 2003; 57(4): 231–2.
26. Krstić D, Krstić J, Krstić S, Mitić-Kocić D. Stress and duration of pregnancy. *Acta Facultatis Medicae Naissensis*, 2006; 23(2): 65–8.



## UTICAJ PRENATALNOG STRESA NA NAČIN ZAVRŠAVANJA POROĐAJA

**Dragan Krstić<sup>1</sup>, Sonja Pop-Trajković<sup>2</sup>, Ljiljana Mirković<sup>3</sup>, Darko Marinković<sup>4</sup>, Jelena Krstić<sup>5</sup>**

<sup>1</sup>Opšta bolnica Leskovac, Služba ginekologije sa perinatologijom

<sup>2</sup>Klinički centar Niš, Klinika za ginekologiju i akušerstvo

<sup>3</sup>Klinički centar Srbije, Beograd, Institut za ginekologiju i akušerstvo

<sup>4</sup>Opšta bolnica Užice, Ginekološko-akušerska služba

<sup>5</sup>Opšta bolnica Leskovac, Služba medicinske biohemije

E-mail: adela@ptt.yu

**Kratak sadržaj:** Cilj rada je da dokaže adaptaciju porođaja na kvalitet života u okruženju trudnice, uticajem prenatalnog stresa na varijabilnost biološkog trajanja trudnoće. Metodologija i izbor pacijenata: Istraživani su učestalost carskog reza (sc), nalaz na prijemu u porodilište kod trudnica sa prethodnim sc i dužina trajanja gravidarne amenoreje pre, tokom i posle bombardovanja, kao perioda niskog kvaliteta života u kome su trudnice bile izložene stresu. Podaci su prikupljeni retrospektivno iz istorija bolesti akušerskog odeljenja opšte bolnice u Leskovcu. U ovoj bolnici nalazi se jedino porodilište za 250.000 stanovnika Jablaničkog okruga na jugu Srbije u kome se obavi oko 2300 porođaja godišnje. Studija uključuje 1448 porođaja u periodu 24. mart – 9. jun, godinu dana pre, tokom i godinu dana posle NATO bombardovanja Jugoslavije 1999-e godine. Podaci su statistički obrađeni  $\chi^2$  i Kolgomorov-Smirnovim testom i prikazani grafički korišćenjem programa Microsoft Excel. Rezultati i diskusija: Učestalost sc značajno pada, a vaginalnih porođaja posle prethodnog sc (VBAC) raste tokom bombardovanja u odnosu na isti period prethodne i naredne godine. Nalaz na prijemu u porodilište kod trudnica sa prethodnim sc i vreme porođaja u odnosu na očekivani datum ukazuju na raniji spontani početak terminskog porođaja (biološki kraće trajanje trudnoće) kao uzrok ove pojave. Zaključak: Mehanizmi prenatalnog stresa skraćuju biološko trajanje trudnoće i time porođaj trudnice sa niskim kvalitetom života čine bržim, lakšim i bezbednijim sa manje indikacija za SC.

**Ključne reči:** Trudnoća, carski rez, rat, stres, adaptacija