

## STRESS – THE RISK FACTOR IN THE LIP AND PALATE CLEFT DEVELOPMENT

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Lip and palate cleft (cheilognathopalatoschisis) is most often congenital defect that affects craniofacial region. It is characterized by a difficult clinical presentation. The etiology is multicausal and not yet fully understood. The examination of numerous etiological factors imposed the need to study the role of stress in the development of lip and palate cleft. This is all the more important for the socioeconomic factors that characterized our society in the last years, after bombardment, poverty, higher divorce rate, and more family violence. The aim of this paper was to establish the importance of stressful events and their role in the development of lip and palate cleft. The examination included children born from March 1999 (time of war in this area), till December 2003, as well as their mothers. The study group comprised 96 children with the lip and palate cleft anomaly, and the control one included 142 healthy children. The chosen examinees were not under the influence of other etiological factors, such as heritage. The examination was conducted using a questionnaire containing questions related to stressful situations in the first trimester of pregnancy. The questions were thus formed so as to be clear to mothers of different levels of education, without expert phrases, except in the cases where it was necessary. The statistical differences between the study and control group were determined using Pearson's  $\chi^2$  test. In the first trimester, the mothers of the study group, in regard to the control group, statistically more often had fears or anxiety ( $p < 0.01$ ), disorganized emotional life ( $p < 0.001$ ), more often psychological harassment ( $p < 0.001$ ), and the presence of any kind of harassment ( $p < 0.001$ ). The presence of stress was also greater in the study group, on the significance borderline in relation to the control group.

The stressful situations to which mothers of the study group were exposed are in correlation with the increase of the children with lip and palate cleft. *Acta Medica Medianae 2007;46(4):15-19.*

**Key words.** stress, lip and palate cleft

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### Introduction

What distinguishes the lip and palate cleft from other hard, innate embryo defects is the fact that due to the distorted muscle adherence, this anomaly can develop to monstrosity. In the past, children with clefts arose interest of both scientists and artists, and of uneducated people, drawing attention to themselves with their almost grotesquely deformed faces. The anomaly can rarely be determined while the baby is still in the mother's stomach, but is always diagnosed at birth. It is a serious problem, and the difficult clinical picture that is associated with this deformity demands prompt, expert, and long

lasting treatment, often even beyond legal age. The anomaly is characterised with the loss of continuity of various structures of orofacial system: lips, alveolus crest, and soft palate (1). The part with the cleft is in turn a part of other facial structures, and therefore changes the frontal part of the mouth, nose, and the whole face. Palate cleft interrupts the continuity of nasal cavity, teeth, and pharynx. There are many cleft classifications, and the hardness of the clinical picture varies. The easiest clinical picture is of barely seen clefts (e.g. lip pseudocleft), hard bilateral lip cleft, alveolus crest and palate, and the hardest clinical picture is of slanted facial clefts. It occurs in all parts of the world; most often in Japan, and in our country, one child per every 750 to 1000 newly borns has some kind of a cleft. They can appear isolated (nonsyndrome clefts), or as parts of one of 400 or more syndromes related to orofacial clefts (syndrome clefts) (2). The mechanism of their development is known (the result of not growing together of maxillary with nasal-frontal process), as well as

time period of development between 4th and 12th week of intrauterine life. However, the causes of lip and palate cleft development are still a riddle. Besides genetics, virus infections, taking some drugs, even smoking, can be etiological factors. Stress as a risk factor in the anomaly development has been confirmed in many studies (3,4,5), and has been the subject of our research.

### Aim

The aim of this study was to determine the relationship between various stressful events in the life of a pregnant woman with the development of lip and palate cleft in their children.

### Method

The examination included children born from March, 1999, (the time of war in this area), to December, 2003, as well as their mothers. The study group was comprised of 96 children with lip and palate anomalies, all treated at the Gynecology Clinic in Nis (Neonatology Ward), VMA (Military Medical Academy) Belgrade (Plastic Surgery Institute), Institute for Mother and Child Protection – Novi Beograd, and Children's Clinic in Tirsh Street, Belgrade. The control group comprised 142 healthy children. This group was formed in three Nis kindergartens. Their age corresponded to the age of the examined group. The chosen examinees were not under the influence of other etiological factors (e.g. genetics). The examination was conducted with questionnaire that contained questions related to stressful situations in the first three months of pregnancy. The questions were thus formulated so as to be clear for mothers of different levels of education, without expert terminology, except in the cases where it was necessary.

The statistic processing of the obtained data was done using analytical and descriptive method. The data were grouped and graphically represented. The statistical differences between the study and the control group were determined with Parson  $\chi^2$  test.

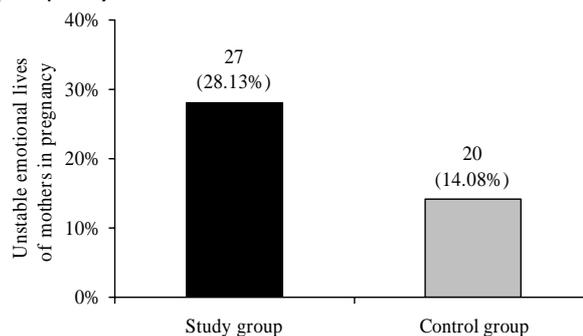
### Results

Our investigation focused on the influence of stress on the occurrence of lip and palate cleft in children, through the emotional life of pregnant women, the presence of stress, long fear or anxiety, and physical and mental abuse during pregnancy.

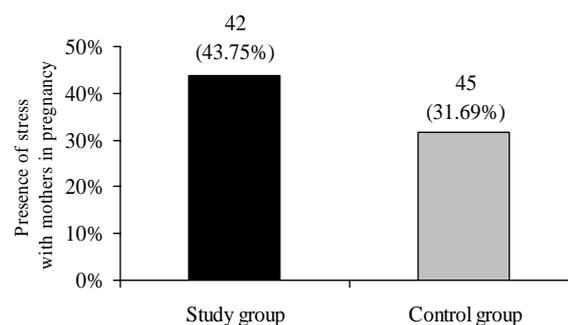
One third of the mothers with children with clefts stated they did not have a stable emotional life - 27 (28.13%), which, in comparison with the control group - 20 (14.08%), produced statistically significant difference ( $p < 0.001$ ) (Graph 1).

High percentage of mothers from the study group - 42 (43.75%) was under stress in the first three months of pregnancy, which, compared with the control group is 45 (31.69%), and is on

the borderline of being significant ( $p = 0.058$ ) (Graph 2).

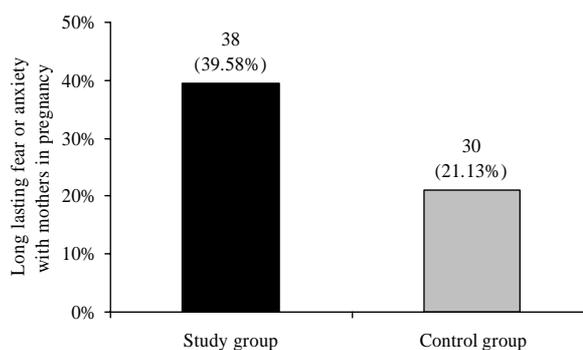


Graph 1. The percentage presentation of unstable emotional lives of mothers during pregnancy



Graph 2. The percentage presentation of the presence of stress in mothers during pregnancy

In the study group 38 (39.58%) mothers felt fear and anxiety during pregnancy. Compared with the answers of mothers from the control group, we determined that the mothers of the study group had statistically significant presence of fear or anxiety ( $p < 0.01$ ) (Graph 3).



Graph 3. The percentage presentation of the long-lasting fear or anxiety in mothers during pregnancy

The investigation also included the occurrence of physical or mental abuse of mothers during pregnancy. None of the examinees of either study or control group were physically abused during pregnancy, but in the study group there were 6 (6.25%) mothers exposed to physical abuse associated with mental. Far higher percentage of psychological abuse is observed in the study group - 13 (13.54%) mothers in relation to 2 (1.41%) mothers from the control group. High percentage of mothers from the

control group - 136 (95.77%), were not exposed to any kind of abuse, while that number in the study group is much smaller - 74 (77.08%), (Table 1). Compared with the control group, mental abuse is much more present in the study group ( $p < 0.001$ ). Also, generally speaking, the presence of any kind of abuse during pregnancy was statistically higher in the study group ( $p < 0.001$ ).

Table 1. Causes of stress during pregnancy

Causes of stress	Study group		Control group	
	n	%	n	%
Physical abuse	–	–	–	–
Mental abuse	13	13,54	2	1,41
Physical and mental abuse	6	6,25	–	–
Negates existence of stress	74	77,08	136	95,77
No answer	3	3,13	4	2,82
Total	96	100,00	142	100,00

## Discussion

Based on literature review, there are numerous studies dealing with the effect of stress on the occurrence of deformities in animals. However, a small number of studies have dealt with this problem with people. Human studies that researched the potential relationship between stressful events and anomalies with the offspring, report on the increased risk of anomalies in children of mothers who had various kinds of stress during pregnancy (5).

Adams et al., used the scale of life events as a method for marking stress. They conducted the research in Georgia. They reported experiencing 2 or 3 stressful events during the period before and around conception to be related with the coefficient of probable frequency OR of 2.4, for the baby to be born with an innate defect (3).

In their research, Czeizel et al., treated stress only as a catastrophic events (6).

Carmichael and Shaw in California conducted a large study that was to examine the effect of stress in pregnancy as a risk factor in the cleft occurrence. The collected data were of 662 mothers with orofacial clefts, and 734 mothers in the control group. Mothers were examined about the period around conception (from the first month before conception) to the end of the third month of pregnancy. Women were asked questions about the loss of a dear person, splitting up with a partner, existential problems (e.g. loss of a job), in the period around conception and the first three months of pregnancy. Their results showed that during the four-month-period around conception, 14,5% of mothers reported the death of a close person, 16.1 % that they or someone close to them divorced, and 9,3% that they or someone close to them lost their job (4).

Based on their research, Carmichael and Shaw concluded that each group with clefts

showed higher frequency related with stressful events. The relationship of isolated palate cleft with stress was limited to women who were not obese, and was stronger among women who reported taking alcohol (5 or more drinks on an occasion). They noticed also a potentially higher risk for clefts with the increase in the number of stressful events, and the higher correlation between stress and the occurrence of clefts in women with lower education. They related that with the fact that the lower education subsumes lower social and economical status (e.g. higher percentage of smoking, weaker immunity, chronic stress, ...) which can increase the influence of stressful events onto fetal development. The authors believe that teratogenic effects of alcohol can be stronger in the presence of stress. In the end this study suggests that women who have experienced stressful events around conception or in early pregnancy bear a higher risk of delivering babies with orofacial defects (4).

Kopelman et al, noticed that there is no connection between the occurrence of cleft and stress in obese women. They explain that obesity is related to the lower activity of stress system (7).

Our investigation focused on the effect of stress on the occurrence of lip and palate cleft in three wholes. Mothers were first asked if during pregnancy they had peaceful and stable emotional life (Graph 1).

Then mothers were asked directly if during, and especially in the first three months they had been under stress. At that point we specified the direct causes of stress (bombing, loss of a job, unsolved residential problem, the death of a close relative, attending a funeral, traffic accident, leaving of a close person to war), but we left the possibility of stating some other reason. As an answer we got a high percentage of mothers from the study group - 42 (43.75%) that were under stress during pregnancy, which, in comparison with the control group, is on the borderline of being significant ( $p = 0.058$ ). It should be noted that the number of mothers in the control group that answered the same way is not irrelevant - 45 (31.69%) (Graph 2).

However, it should be emphasized that these results, in the presence of stress, in our population were to be expected, regarding the fact that our examinees were pregnant immediately before, during, or shortly after the bombing and war in our country, which largely contributed to the stressful situations during pregnancy. This is in line with the findings reporting that only in our region, 350 attempts of suicide were registered, 64% of which were women (8). The fact that stress could not be measured with any definite unit made the examination of this risk factor in the lip and palate cleft development much harder. The researchers of earlier studies encountered this problem, too. It is well-documented that stress has a role in the disturbance of numerous physiological processes, influencing also the occurrence of lip and palate cleft (9,10,11). However, most of mothers of the study group insisted that the stress due to bombing certainly

contributed, but was not the exact cause of this difficult anomaly. Working on this research, we encountered highly moving testimonies on the fear that lasted even up to 24 hours, followed with insomnia, shivering, teeth chattering (12). Various fears were enumerated: fear for one's life, the lives of children, of husband or brother that were in the war zone. The sound of sirens was especially stressful for the examinees. It is interesting that the fear for the unborn baby was not the priority. It appeared only after the delivery of the baby with the obvious anomaly on the face. From such pregnancies (most often from Kosovo) babies were born with hard slanted facial clefts, rarely described in literature. Many of the examinees stated that during stressful situations they smoked heavily, ate less food, which in literature is described as a potential stress mechanism to the fetal development. Stress can lead to the harmful behavior of women oriented to overcoming the situation (higher use of certain substances, lower food quality,...) which indirectly influence the development of fetal deformation (13).

Apart from stressful situations connected with bombing, in our research, another problematic moment appears. Namely, in the study group 6 (6.25%) women were subjected to physical abuse during pregnancy, which is directly against basic morality and which further actualises this problem as family violence is significantly on the increase (Table 1). Besides physical abuse, there

was a negligible number of women - 13 (13,54%) of the study group who were under constant stress due to psychological abuse during pregnancy, which certainly initiated the mechanism of stress affecting the fetus development. We believe that the number of pregnant women who were abused in this way is even larger if we take into account the factor of concealing the facts (patriarchal upbringing) which in our area is still largely present.

Based on all this, we can conclude that the presence of stress had a large role in the appearance of lip and palate cleft in our examinees, which is in line with the examinations performed by other researchers (3,4,5).

### Conclusion

Stressful situations to which the mothers of the study group were exposed by being in the area of the most intense war activities had for a consequence a significant effect onto the occurrence of lip and palate cleft of their children. However, during the course of investigation it turned out that this is a dominant, yet not the sole cause of stress in the examined pregnant women. It is most concerning that family violence is largely present and that as such it disturbs the stable life of pregnant women which can lead to the appearance of fetus deformities of the lip and palate cleft type.

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## STRES - FAKTOR RIZIKA U NASTANKU RASCEPA USNE I NEPCA

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Rascep usne i nepca (cheilognathopalatoschisis) je najčešći urođeni defekat koji pagađa kraniofacijalnu regiju. Karakteriše se jako teškom kliničkom slikom. Etiologija je multikauzalna i do današnjih dana je ostala nedovoljno rasvetljena. Ispitujući mnogobrojne etiološke faktore, nametnula se potreba za proučavanjem uloge stresa u nastanku rascepa usne i nepca. Ovo je utoliko aktuelnije, ukoliko se sagledaju socioekonomski faktori koji karakterišu našu društvenu zajednicu poslednjih godina, posle bombardovanja, siromaštva, povećane stope razvoda brakova i porasta nasilja u porodici. Cilj ovog rada je utvrđivanje značaja stresnih događaja i njihove uloge u nastanku rascepa usne i nepca. Ispitivanjem su obuhvaćena deca rođena od marta 1999. (vreme ratnih dejstava na našim prostorima) do decembra 2003, kao i njihove majke. Studijsku grupu je činilo 96 dece sa anomalijom rascepa usne i nepca, a kontrolnu 142 zdrave dece. Izabrani ispitanici nisu bili pod delovanjem drugih etioloških faktora (npr. nasleđe). Ispitivanje je sprovedeno putem upitnika koji je sadržao pitanja vezana za stresne situacije u prvom tromesečju trudnoće. Pitanja su formulisana tako da su bila jasna za majke različitog nivoa obrazovanja, bez korišćenja stručnih izraza, osim u slučajevima gde je to bilo neophodno. Majke studijske grupe su u prvom tromesečju trudnoće, u odnosu na kontrolnu grupu, statistički češće imale prisustvo straha ili zebnje ( $p < 0,01$ ), nesređeniji emocionalni život ( $p < 0,001$ ), veću zastupljenost psihičkog maltretiranja ( $p < 0,001$ ), kao i prisustvo bilo kog tipa maltretiranja ( $p < 0,001$ ). Prisustvo stresa je bilo takođe veće u studijskoj grupi, na granici značajnosti u odnosu na kontrolnu grupu. Stresne situacije kojima su bile izložene majke studijske grupe u korelaciji su sa porastom broja dece sa rascepom usne i nepca. *Acta Medica Medianae 2007;46(4):15-19.*

**Ključne reči:** stres, rascep usne i nepca