

## OUTCOME OF THE PREGNANCIES AFTER UTERINE CERVIX CONIZATION

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**Summary.** *Constant rise of incidence of intraepithelial uterine cervix lesions in young patients implies a larger number of therapeutic surgical procedures. The paper aims to assess the risk of such surgical procedures on later pregnancy and delivery. The paper is a retrospective study performed at the Clinic of Gynecology and Obstetrics in Niš. The study enrolled 30 pregnant women in the experimental group with conization of the uterine cervix in their history, and 90 pregnant women without history data on previously performed conizations. The investigation demonstrated a significantly higher percentage of deliveries before 37 week of gestation in our experimental group – 20% vs 5.5% in the control group. Deliveries in experimental group more commonly started with preterm rupture of membranes (pPROM) – in 13.3% - while the corresponding percentage in control group was only 2.22%. Related to operative completion of delivery with cesarean section, there were no significant differences between the groups (6.6% vs 3.3% in experimental and control group, respectively). There was a statistically significant difference in cervix injury during labour in experimental (10%) compared to control group (1.1%). Uterine cervix conization represents a risk for preterm labour in late pregnancy. In these women, delivery more commonly starts with preterm rupture of membranes and uterine cervix injuries are more common. Therefore, conization should be utilized only if strictly indicated in young patients, and those with conization should be closely monitored.*

**Key words:** *Conization, pregnancy*

### Introduction

Intraepithelial cervical lesions occur in women in their generative years. These changes have been more and more common lately, with the yearly increase in incidence of around 2%. According to the American Cancer Registry, high grade intraepithelial lesions occur in 31.4 per 100.000 (1).

What is especially important is the fact that incidence in younger women is rising. In the 1950s intraepithelial lesions commonly occurred in women aged 35-40 years. These lesions can nowadays be identified even in girls below 15. They reach the highest prevalence (29/100.000) in women aged 24-29, i.e. those who have not fulfilled their generative function. These lesions are mainly surgically treated – with locally destructive or excision techniques in out-patient or hospital environment. Diagnostic and therapeutic approaches evolved with better understanding of the etiology and biological background of the lesions, as well as with advancing diagnostic and therapeutic technology. These changes led to changes in the categorization of the degree of radicality of therapeutic procedures. Some procedures which were regarded as conservative in the past, have now been regarded too radical and unacceptable.

Though individualized treatment approach is mandatory in women with intraepithelial lesions (differences regarding the age, reproductive status/parity, disease

site), there are some general recommendations. The attitude is prevailing regarding the most sparing but radical enough treatment which eradicates the lesion but does not mutilate reproductive organs. Though we may strictly observe such an attitude and apply novel conservative techniques (laser, LETZ), surgery nevertheless reduces the volume of the cervical tissue, it reduces the length of the cervical channel, leading to specific, local immunologic and fibrotic tissue reactions, cervical stenoses (in 1-17%), preterm labour, and infertility (in about 4%) (3).

The most popular surgical treatment approach for intraepithelial lesions was cold knife conization and, later on, out-patient locally destructive methods such as cryotherapy and electrocauterization. Laser therapy was introduced during the 1980s in the developed world, and in 1990s loop electrosurgical excision of the transformation zone (LETZ) was extensively utilized. This method gained popularity as the first step in diagnostic work-up and treatment of abnormal colposcopic and cytologic findings ("first visit" or "see-and-treat" approach). However, there are no long-term studies which could confirm the positive effect of LETZ on the preservation of fertility. On the contrary, there are papers which suggest that this treatment modality can increase the percent of infertility and preterm labour, indicating that this approach cannot be routinely recommended as the "first visit" treatment.

Since cervical intraepithelial lesions predominantly occur in fertile female population and even in adolescents, and in view of the fact that spontaneous regression occurs in 66% of the mild lesions and in 35% of those more severe, future investigations will focus on the identification of the most conservative treatment modality.

**Aim**

Aim of this paper is to establish the risk of conization on the outcome of pregnancy and delivery.

**Material and methods**

A retrospective study was organized at the Clinic of Gynecology and Obstetrics in Niš. The study enrolled 30 pregnant women in the experimental group with conization of the uterine cervix in their history. The documentation, patient history and protocols provided us with the data later processed with chi-square test and presented graphically and in tables. Ninety pregnant women delivered at the Clinic of Gynecology and Obstetrics in Niš without history data on previously performed conization comprised our control group.

**Results**

Table 1. demonstrates the percentage of pregnancies in experimental group with delivery before 37 week to be 20% - more compared to controls (only 5.55%). The difference is statistically significant ( $\chi^2 e = 5.62 > \chi^2 0.05 = 3.841$ ).

Table 1. Gestational age at the time of delivery in experimental and control groups

Gestational age	Experimental group	Control group
Below 37 weeks	6 (20%)	5 (5.5%)
Over 37 weeks	24 (80%)	85 (94.5%)
Total	30 (100%)	90 (100%)

The percentage of newborns with body weight below 2500 g is presented in Table 2. It is also higher in experimental subjects (13.33%) compared to controls (4.44%), but the difference is not statistically significant ( $\chi^2 e = 2.78 < \chi^2 0.05 = 3.841$ ).

Table 2. Birth weight

Birth weight	Experimental group	Control group
Below 2500 g.	4 (13.3%)	4 (4.4%)
Over 2500 g.	26 (86.7%)	86 (95.6%)
Total	30 (100.0%)	90 (100.0%)

Table 3 demonstrates that the percentage of preterm rupture of membranes (PPROM) in experimental group is higher (13.33%) compared to controls (2.22%) and that the difference is of statistical significance ( $\chi^2 e = 5.16 > \chi^2 0.05 = 3.84$ ).

Table 3. Distribution of pPPROM patients (preterm rupture of the membranes)

PPROM	Experimental group	Control group
With PPRM	4 (13.3%)	2 (2.22%)
Without PPRM	26 (86.7%)	88 (97.77%)
Total	30 (100.0%)	90 (100.0%)

The percentage of surgically completed (Cesarean section) deliveries is presented in Table 4; that percentage is only slightly higher in the experimental group (6.6%) compared to controls (3.3%). The difference is not statistically significant ( $\chi^2 e = 0.60 < \chi^2 0.05 = 3.84$ ).

Table 4. Patient distribution based on the mode of delivery completion

Delivery completion	Experimental group	Control group
Cesarean section	2 (6.6%)	3 (3.33%)
Vaginal	28 (93.4%)	87 (96.6%)
Total	30 (100.0%)	90 (100.0%)

Table 5 indicates that cervical ruptures were more common in the experimental group (10%), while only 1.1% of those in the control group had cervical injury. There is a statistically significant difference ( $\chi^2 e = 5.49 > \chi^2 0.05 = 3.84$ ).

Table 5. Patient distribution on the basis of uterine cervix rupture after delivery

Cervical rupture	Experimental group	Control group
With rupture	3 (10%)	1 (1.1%)
Without rupture	27 (90%)	89 (98.8%)
Total	30 (100%)	90 (100.0%)

**Discussion**

Tables 1 and 2 demonstrate the level of risk of the anamnestic data on previously performed conization of the uterine cervix regarding preterm labour (before week 37) and low birth weight (below 2500 g). Table 1 clearly indicates that cervical conization is a risk for later preterm labour – 20% of the experimental group subjects. Low birth weight (<2500 g) was also more common in the experimental group (13.3%) but the difference was not statistically significant.

The percentage of newborns requiring neonatal intensive care unit – NICU – is not presented in tables, since only one child in the experimental group with birth weight below 2000 g required intensive care for respiratory distress syndrome (RDS).

Literature data demonstrate that the percentage of preterm labour after cold knife conization is 14% vs 5% in controls (4). In some papers the proportion is 22.4% vs 6.6% in controls (5). If LETZ surgery is performed, the percentage of preterm delivery is slightly lower – 11% for experimental, and 7% for control subjects. The percentage of children born with body weight of less than 2500 g was also lower with this treatment than with

cold knife conization (8% vs 4% in experimental and control groups respectively) (4). These data demonstrate that LETZ is a more conservative treatment for cervical changes, inducing less cervical volume reduction and shortening of the cervical channel, and it is the treatment of choice in younger patients with squamous epithelial lesions of the uterine cervix. However, the fact that this treatment modality leads to higher percent of preterm labour requires an individualized, critical approach.

Some authors have tried to determine the statistical value of median for clinical gestation and body weight of newborns in experimental and control groups. The median values for clinical gestation at delivery was 39 for experimental and 40 for control group, while body weight median was 3330 for experimental and 3630 for control group (6).

Table 3 presents the incidence of preterm rupture of the membranes (pPROM) in experimental and control groups. We came to a conclusion that in experimental examinees delivery more frequently started with preterm rupture of membranes (13.33%). The PPRM percentage in experimental subjects in the literature is higher too – 5%, vs 2% in controls. In some more recent papers we may also note a greater difference – 17.1% vs 2.6% in experimental and control groups, respectively (5). These data, regardless of some percentual discrepancies, demonstrate that pregnant women with history of conization more commonly have premature labour starting with premature pPROM.

Our statistical analysis of the data did not include the factors of age of the women, parity nor smoking, since many of the recent papers have demonstrated that these are independent factors which do not alter significantly the total percentual difference between experimental and control groups (7).

This study did not address the issue of size of the removed uterine cervix cone since we did not have the pathology data. Though the data on the issue are different regarding the "critical" size of the removed cone for preterm labour, median calculated length of 10 cm or more is of statistical significance for subsequent preterm labour (8). Measurement of the cervical channel by transvaginal sonography (TVS) during a pregnancy can inform us indirectly about the length of the cervical channel remaining after conization. Literature data also point out that there is a direct link between the risk of preterm labour with the size of the remaining cervical channel. Depending on the surgical procedure administered, the length of the remaining cervical channel varies. In control subjects the length is 4.21 cm on the average, while in pregnant women previously treated with conization cervical channel is 3.54 cm long, and in loop treated women it is 3.69 on the average. Minimal shortening of the cervical channel associated with statistically more common preterm labour is 3.78 cm. The length of 3.0 cm is a cut-off value with predictive value of 53.8% and negative predictive value of 95.2% for preterm labour in a pregnancy (9).

The significance of an early cerclage in the second pregnancy trimester was not statistically processed in this paper since all of the experimental group subjects had preventive cerclage after vaginal-cervical swabs checks. Furthermore, literature data point out that preventive cerclage does not influence the increase of gestational age of the newborns after postconization pregnancies (10).

A special issue in our study was the mode of delivery completion and the percentage of uterine cervix injuries in pregnant women with previous cervix conization. The data in Table 4 demonstrate that the proportion of surgically finalized pregnancies (Cesarean section) is only slightly higher in experimental subject (6.6%) vs controls (3.3%). There was no statistically significant difference.

The proportions of Cesarean sections in the literature in more distant past were higher in patients with previous conization (even up to 25.5%) (10).

From the data in more recent literature, the tendency of reduction of the numbers of Cesarean section in experimental groups has been evident. Some studies from 2006 demonstrate the percentages similar to ours (9% for experimental and 3% for control subjects) (4).

What was obviously more common are cervical ruptures during delivery in experimental subjects. The percentage of cervical ruptures was around 10%, while control subjects had cervical ruptures in only 1.1%. The literature data are similar to our own (8.8% vs 1.3% in experimental and control groups, respectively) (5).

The proportion of precipitant deliveries (those lasting <2 h) was not the issue of interest in our study. Literature demonstrates that vaginal delivery in women with previous conization is shorter by 5.5 to 7 hours compared to control pregnancies, and that percentage of precipitant deliveries is up to 13% (11).

## Conclusion

This study of ours, together with the relevant literature data, demonstrates that treatment of intraepithelial lesions of the uterine cervix in younger women increases the risk of preterm labour in subsequent pregnancies.

Preterm labour in women with history of cervical conization more commonly starts with preterm rupture of membranes.

Surgical completion of pregnancy is not significantly more common in pregnant women with history of cervical conization, but in these patients cervical rupture is more common.

Because of this, we believe that uterine cervix conization should be very sparingly used in younger women and those with history of conization should be closely observed.

We have more and more information confirming that cervical epithelial lesions, especially low grade ones, commonly spontaneously regress into normal finding. Some modern detection methods, such as HPV typiza-

tion and specific genetic and immunologic specific prognostic markers (Cytoactive test), can be of use in prediction and selection of the lesions with high risk of progression and they require surgical management. And there are others, which require only surveillance or, possibly, ablative treatment. The tests to detect progressive lesions are commonly based on the detection of specific protein defensive immunologic factors produced by the cells in the struggle with HPV infection. The lesions

with such proteins commonly spontaneously resolve and require just monitoring.

What is most important in the treatment of young women with cervical intraepithelial lesions is individualized approach to treatment, based on the experience and ability of the physician doing colposcopy to find out the most appropriate balance between the need to eradicate the disease and the need for minimal defect and disturbance of cervical anatomy.

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## ISHOD TRUDNOĆA NAKON KONIZACIJE GRLIĆA MATERICE

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Kratak sadržaj: *Stalni porast incidence intraepitelnih lezija grlića materice kod mladih pacijentkinja, povećava i procenat hiruških procedura koje se primenjuju u njihovom lečenju. Ovaj rad je imao za cilj da ispita rizik ovakvih hiruških procedura na kasniju trudnoću i porođaj. Radi se o retrospektivnoj studiji sprovedenoj na Ginekološko akušerskoj klinici u Nišu. Ispitivanje je obuhvatilo 30 trudnica eksperimentalne grupe koje su anamnezi imale urađenu konizaciju grlića materice i 90 trudnica kontrolne grupe bez anamnestičkog podatka o ranije urađenoj konizaciji. Istraživanje je pokazalo statistički značajno veći procenat porođaja pre 37 nedelje gestacije trudnica eksperimentalne grupe 20% prema 5,5% u kontrolnoj grupi. Porođaji u eksperimentalnoj grupi su statistički češće počinjali sa pretermnim prevremenim prsnućem plodovih ovoja (PPROM) i to u 13,3% ispitanica, dok je procenat PPRM –a u kontrolnoj grupi bio samo 2,22%. U odnosu na operativno dovršavanje porođaja carskim rezom nije postajala statistički značajna razlika između ispitanica eksperimentalne i kontrolne grupe (6,6% prema 3,3% u korist eksperimentalne grupe). Postajala je statistički češća pojava povreda cerviksa u porođaju ispitanica eksperimentalne grupe 10% prema 1,1% kod porodilja kontrolne grupe. Konizacija grlića materice predstavlja rizik za pojavu prevremenog porođaja u kasnijoj trudnoći. Kod ovih trudnica porođaj češće započinje sa prevremenim prsnućem plodovih ovoja i češće su u porođaju povrede grlića materice. Zbog svih ovih razloga konizaciju kod mladih pacijentkinja treba strogo indikovano koristiti a trudnice sa prethodno urađenom konizacijom intenzivno pratiti.*

Ključne reči: *Konizacija, trudnoća.*