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ORIGINAL PAPER

Cervical Length Measured by Transvaginal Ultrasonography and Cervicovaginal Infection as Predictor of Preterm Birth Risk

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ABSTRACT

Introduction: The study shows possibilities of transvaginal sonographic measurement of the cervix in prediction of premature birth risk. **Goals:** The aim of the study was to follow up the cervical length in the pregnant from 16th to 37th week, as well as to do a microbiological analysis of the vaginal and cervical flora and to identify relation between the cervical shortening and microbiological flora as well as with a premature birth. **Material and methods:** The investigation was conducted as a prospective study on two groups of female patients in Clinical Centre of Banja Luka. In the high risk group we had 8% of patients with cervical length below than 15mm, 30% of patients with cervical length from 15 to 25mm and 62% of patients with cervical length bigger than 25mm. In the low risk group we had no patients with cervical length below 15mm, 95% of patients had cervical length bigger than 25mm and 5% of patients had cervical length from 15 to 25mm. **Results:** The regression coefficient of the cervical length in the high risk group was 0.44mm, while in the low risk group it was 0.26mm. In the high risk group 67.56% patients had a positive cervical smear finding, while in the low risk group it was 4%. A high premature birth (defined as birth before 36.6 weeks) incidence of 50% was presented in patients with cervical length below 15mm. In the group of patients with cervical length up to 25mm the premature risk incidence was 10.52±0.05. In the high risk group of patients with a positive cervical smear finding, regarding the cervical length the percentage was as follows; in the subgroup of 15mm length 88,89±11,87, in subgroup from 15 to 25mm was 62,07±11,43 and in the subgroup bigger than 25mm, 60.06±8.05. **Conclusion:** By the analysis of the first and second goal of our study we can conclude that ultrasound assessment of cervical length is simple and feasible in the 16th week of pregnancy in both groups, with high and low risk. The length of the cervix in this period is shorter in the high risk group compared with the low-risk group. This difference was not statistically significant, however, it clearly demonstrated connection between shortened length of the cervix with the preterm birth. A regression analysis shows that the shortening of the cervix length is more frequent in high risk group which is to be expected, bearing in mind that in this group, the risk of preterm delivery was significantly higher.

Key words: cervicometry, preterm birth, cervical length.

1. INTRODUCTION

Ultrasound cervicometry is a method for estimating the length of the uterus, which has its place in the prediction of late miscarriage and preterm birth. These results confirmed number of authors, and it has been proven through the first and second predefined goal of this study. In studies published the cervicometry was indicated as better method than bimanual examination in screening of high-risk groups for preterm birth (1). Ultrasonic measurement of cervical length separates a group of pregnant women with threatening preterm birth, and opens the possibility of timely responses, thus avoiding unnecessary cerclage with possible adverse consequences. As in most medical dilemmas, as well as this, there are still no standardized criteria for ultrasound finding of cervix weakening. Currently the most important parameter is the shortening of the cervix length, but the exact values still varies.

2. GOAL

The goal of the research is defined by:

- Estimate the length of the cervix at 16 weeks, depending on the risk group (high and low);
- Monitor the length of the cervix in pregnant women in both groups (high and low risk) at 16 week to week pregnancy;
- Microbiological analysis of vaginal and cervical microbial flora by taking microbiological samples—swabs, and observe any correlation between shortening of the cervix and microbial flora, and with the occurrence of preterm birth;
- Evaluate the association of shortened cervix with preterm birth.

3. MATERIAL AND METHODS

This prospective study, which was conducted in the Clinic of Gynecology and Obstetrics, Clinical Center

of Banja Luka. Part of pregnant women enrolled in the trial was hospitalized at the Department of Conservative gynecology because of various indications that did not have an impact on our testing, while part was examined as ambulatory patients at the Clinic of Gynecology and Obstetrics, Clinical Center of Banja Luka.

The respondents were divided into two groups: experimental group or a group at high risk for preterm birth and a control group or a group of low risk for preterm birth. Criteria for inclusion in the high-risk group were: pregnant women with premature birth or late miscarriage in a previous pregnancy, pregnant women with previous artificial or medically indicated abortions, and women with surgeries of the cervix, in pregnant women with suspected or proven cervical infections.

4. RESULTS

In the period from January 1st 2007 to September 1st 2010 the study included 200 women. They are selected by criteria defined as a high-risk group (n=100), and a low-risk group (n=100). Each group began with participation in the study after taking the anamnesis at first examination in 16th week of pregnancy. It included classic gynecological examination, transvaginal ultrasound examination with measurement of cervical length, taking a cervical smear, and fetal biometry with routine laboratory tests as defined by the protocol.

Group	Length of the cervix	%	±	S _%
High risk	Less than 15 mm	8.0	±	0.02
	From 15 to 25 mm	30.0	±	0.04
	Longer than 25 mm	62.0	±	0.04
Low risk	Less than 15 mm	-	-	-
	From 15 to 25 mm	5.0	±	0.06
	Longer than 25 mm	95.0	±	0.02

Table 1. Relative frequency of subjects observed by analytical subgroups with different lengths of cervix in high-risk and low-risk groups for preterm birth

Risk group	High risk (%)	Low risk (%)
Positive finding	67.56 ± 7.80	4.00 ± 1.95
$t_{exp.} = 7.901$		
$t_{0.05} = 1.667$		
$t_{0.01} = 2.381$		

Table 2. Relative frequency of positive cervical smear in both groups

Cervix length	Mean (%)	Standard error
Less than 15 mm	88.89	± 11.87
From 15 to 25 mm	62.07	± 11.43
Longer than 25 mm	60.06	± 8.05

Table 3. Relative frequency of positive cervical smears according to the length of the cervix in the high risk group and its statistical significance

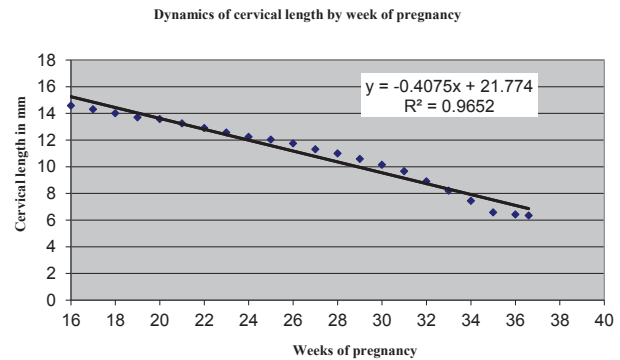


Figure 1. The dynamics of shortening the cervix length o by week pregnancy from the original value of <15 mm measured at 16 weeks of pregnancy in high risk group

Isolated pathogen	%(n)
Enterococcus	42.85(27)
E. Coli	20.63(13)
Streptococcus	20.63(13)
Gardnerella	6.39(4)
Staphylococcus hom.	3.17(2)
Staphylococcus ep.	3.17(2)
Proteus mirabilis	1.58(1)
Ureaplasma urealiticum	1.58(1)

Table 4. The frequency of isolated pathogens in cervical smears in high risk group

Isolated pathogen	16 week	36.6 week	16w-36.6w in mm
Gardnerella	32.65 ± 2.25	21.40 ± 2.78	11.25
E. Coli	33.44 ± 1.95	23.15 ± 1.27	10.29
Enterococcus	31.21 ± 2.01	21.42 ± 1.52	9.79
Streptococcus	29.97 ± 4.39	20.89 ± 2.59	9.08

Table 5. The difference in the length of the cervix according to the cause of infection in the 16th and 36.6 week of pregnancy

Isolated pathogen	% of preterm birth
Enterococcus	37.5
Staphylococcus	12.5
Streptococcus	12.5
E.Coli	12.5
Without infection	25.0

Table 6. The incidence of preterm birth before 37 weeks depending on the isolated pathogen from cervical swabs in the high risk group.

Cervix length	Preterm delivery in week		
	34-34.6	35-35.6	36-36.6
	%	%	%
<15mm	25	25	50
15-25mm	-	-	100
>25mm	-	-	100

Table 7. Relative frequency of preterm birth in certain weeks, depending on the length of the cervix in high risk group

Respondents	X	±	Sx	t _{exp}
Cervix length up to 25mm	75.00	±	12.31	2.872
Cervix length above 25mm	25.00	±	12.31	

t_{0.05}=1.894 t_{0.01}=2.998

Table 8. Relative frequency of preterm birth, depending on the length of the cervix in high risk group

Respondents in the high risk group	Preterm delivery (X±Sx)	t _{exp}
Microbiological swab positive	87.50 ±	11.69 4.537*
Microbiological swab negative	12.50 ±	11.69

t_{0.05}=2.920 t_{0.01}=6.965

Table 9. Relative frequency of preterm birth, depending on the findings of a positive cervical smear in the high risk group

5. DISCUSSION

In this study we included two groups of pregnant women, a group at high risk for preterm birth (n=100) and a group of low risk for preterm birth (n=100). In the high risk group in 16th week short cervix had 8% of pregnant women, 30% of the truncated normal pregnant women and 62% of them. In the low-risk group 95% of pregnant women had normal cervical length and truncated was of 5%.

Mean values of the cervix length at the high-risk group were 30.8 mm and in the low-risk group 35.0 mm. Thus, the length of the cervix in the high risk group was shorter than it was in the low-risk group. It is expected that the data is first clearly defined in our study, because we know that a history of risk is very important in determining and categorizing the general population of pregnant women with regard to the risk of preterm birth. From our results it is clear that in the high-risk group, defined by previously determined parameters, there is clearly a shorter length of the closed portion of the cervical canal and the length of the cervical canal shows a history of previous miscarriage and/or preterm labor in previous pregnancies is an important fact and risk factor for the next pregnancy. This is a very important observation that has not been clearly defined in other clinical trials and certainly opens up new possibilities for the preparation and design of future studies that will address cervicometry as a method of detection risk group for preterm birth. Dynamics of shortening the door was followed from the 16 to 37 weeks of pregnancy, which was the second goal of our research. The largest regression coefficient in this study were obtained by the group of high-risk long neck above 25mm and he was 0.65 mm, followed by a group of cervix length below 15mm 0.41 and a group of 15 to 25mm where the regression coefficient was 0.27 mm per week. In the group of low-risk weekly regression coefficient was 0.26 mm. These data are also original and very interesting because they were not so far the subject of analysis. In our results is clear that the regression coefficient was higher in the high risk group

than in the low-risk group. It is to be expected because bearing in mind the relatively high average value of cervical length at baseline (week 16), and the connection between the length of the cervix with preterm birth in the high risk group was expected that there must be a significant shortening of the length of the uterus cervix during pregnancy. It was proved in our study that the largest regression coefficient was in the high risk group of pregnant women who have had the longest cervix at 16 week. And this fact with its originality will have an effect on the design of future studies as well as new screening programs screening of pregnant women at risk for preterm birth.

Our results are consistent with the published studies. The study of Hee Lee Yoong and associates, 2009, in the group of low risk for preterm birth cervix length was measured after 22 week and was 35.70 mm, and at 28 week 33.70 mm. There was no significant regression in the length of the cervix (2). And it is relatively expected data, as low risk populations who have not observed an increased incidence of preterm birth and there is no reason for the significantly greater shortening of cervical length of 22 to 28 weeks of pregnancy, and it is expected that by symbolically shortening should come later. In the high risk group cervix length in 15 week amounted to 36mm, in the 20 week 35 mm, and in the 25 week 33.80 mm. In this study has proven that ultrasonic measurement of the cervix length between 16 and 24 week has significance.

Berghella et al. Define ultrasound as a method for assessment of the length of the door, or for the prediction of preterm delivery (3). They pay special attention to proper technique of performance, which is essential for accurate results. Ultrasonic measurement of cervical length in comparison with clinical bimanual examination showed a better diagnostic value to assess the risk of preterm birth in the general population of pregnant women. A classic digital gynecological examination in pregnancy also have been traditionally used in everyday practice and has not proved as effective in detecting cervical weakness, because often the exterior mobility of the cervical canal is wrongly declares pathological condition. There is increasing evidence that the cervicometry can provide very valuable information in support of the weakness of the cervix.

Matijevic et al. conducted randomized controlled study, which followed the diagnostic accuracy of sonographic assessment of cervical length and clinical examination in the second quarter (4). Total of 282 patients, asymptomatic, singleton pregnancy. Experimental group (n=138) and control group (n=144). Shortened cervix was defined as ≤ 24 mm, ≤ 5 percentile. In the control group, Bishop score ≥ 4 is defined as high. Preterm labor is defined as every before 37 weeks. Shortened cervix was found in 6/138 patients (4.3%). Bishop high score in 17/144 patients (11.8 %). The incidence of preterm birth 16/282 patients or 5.7 %. Sensitivity of 57.1 compared to 33.3, the positive

predictive value of 66.7 % compared to 17.6 %. Shortened cervix in relation to the high Bishop score had a 12 times greater chance of preterm birth in low risk group. The conclusion is that ultrasound evaluation has better diagnostic accuracy in predicting preterm birth in relation to digital examination in low-risk group.

In this study, we analyzed the microbial vaginal/cervical flora in both groups, with high and low risk, and the observed correlation between length of the cervix and positive microbial flora with premature birth. In the group of high-risk we had a positive microbiological finding of cervical smear in 67.56 % of patients, while in the low-risk group we had only 4 % of positive findings. In the group with high-risk, short cervix <15mm, positive results of microbiological swabs had 88.89 % of patients, with the shorter cervix length of 15 to 25mm positive swab had 62.07 % and 60.06 % of patients in the group with normal length of the cervix above 25mm. T-test of significance showed a statistically significant higher relative frequency of positive cervical smear findings in the high risk group to low-risk and high-risk groups within the significantly higher relative frequency with cervix lengths below 15mm. This is very important information because it connects the positive microbial flora and the length of the cervix and connecting the two etiological factors of preterm birth—infection and cervical insufficiency. It is not possible to determine which of these two is more important, and/or which appeared before and perhaps benefited to another. It is our opinion that the infection is still what it was favorable for shortening the length of the cervix, as we observed shorter length of the cervix in patients with a positive swab. Also, there needs to bear in mind the fact that the positive results of cervical smear was found before inclusion in the study, or more than 50 % of the women groups at high risk. We tracked the incidence of preterm birth in both groups of patients with positive microbiological findings of cervical smears. In the group of high-risk with cervix length up to 15mm 25% of patients had a positive cervical smear and the birth was after 34week, 25 % in 35 week and 50 % in 36 week. Patients with shortened cervix length with shorter cervix in high-risk group with positive cervical smear positive had preterm births in 36 week. When we analyzed the relative frequency of preterm birth according to the findings of positive microbiological findings of cervical smears, we noticed that 87.50 % had a positive smear and preterm birth, or 12.5% negative cervical smear.

Matijevic et al., In the study of bacterial vaginosis and cervical infections, for prediction of preterm labor, defined any before 37 weeks, and early preterm birth \leq 34 weeks in the group of low risk $n=316$ (5). Vaginal pH was measured by the test glove and cervical length (CL) by transvaginal ultrasound. PH value measured less than 5.0 (95th percentile) and CL larger than 26mm (5th percentile) were consid-

ered normal findings. Of the 14 patients (4.4%) were with higher vaginal pH, and 15 (4.7%) with a shortened length of the cervix. The incidence of preterm birth was 7.2%, while the incidence of preterm birth was 2.5%. The length of the door in the study was significantly correlated with preterm birth but not with early preterm birth. Elevated vaginal pH was a better predictor of early preterm birth of a shortened neck in the group of low risk.

In this study, we followed two groups, a group at high risk with previous preterm births, previous abortions, previous interventions on the cervix, shortening of the cervix and positive microbiological findings of cervical smears. In the low-risk group, were patients that did not have load of previous pregnancies and the proper length of the cervix. In the high risk group controls were made in dependence on the cervix length, so for the patients with shortest cervix < 15 mm we measured by ultrasound cervix length each week, with a length of 15 to 25mm every other week, and with cervix length > 25mm as in the group of low risk every 4 weeks. In the study, we concluded that a group with cervix length below 15 mm had a 50 % incidence of premature births, which was statistically significant compared to the length of the cervix above the 25 mm in high-risk group. If we display cervix length of 25mm as the normal length, and a group of up to 25mm as pathological findings, 75 % of the total number of premature births would be in this group. In this way, by the study we have proved that a group of high-risk patients with short cervix in the 16th week is the one that needs to be monitored as a high risk for preterm birth.

Study of Owen et al. speaks about length of the cervix that has a 3.3 times higher relative risk of preterm delivery (7). The study lasted from March 1997 until November 1999 at nine university medical centers in the United States. Included were 183 patients, singleton pregnancy, which used to have a spontaneous preterm birth before 32 weeks of gestation. The first review was carried out between 14 and 18 weeks of gestation. Sonographic measurement was carried out in two-week intervals. It is also accompanied by the so-called funneling and dynamic cervical shortening. Preterm labor is defined as the one before 35 weeks of gestation. Of the 138 patients, 48 (2%) had a preterm birth before 35 weeks. Cervical length < 25mm at the first sonographic measurement is associated with a relative risk of spontaneous preterm birth of 3.3 (95% confidence interval, sensitivity 19 %, specificity 98 % and positive predictive value 75%). The study concluded that ultrasonographic monitoring of cervical length between 16 and 18 weeks as serial assessments at biweekly intervals has significant predictive value for preterm birth before 35 weeks.

Grgic et al. followed the length of the cervix and gland parameters (QGCS), ultrasound measurement in the second quarter of predicting preterm birth in low-risk populations (81). The prospective study included 278 patients without symptoms of preterm

labor, nulliparous, singleton pregnancies. CL and QGCS were monitored from 16 to 23 weeks of pregnancy. CL \leq 24 mm was defined as shortened. QGCS parameters were: cervical mucus thickens and invasion of cervical glands. Score \leq 1 is defined as low. Shortened cervix was present in 6.1 (17/278) and low QGCS in 5.7 % (16/278). The incidence of preterm birth before 34 weeks was 2.4% (6/278) and between 34 and 37 week 3.2% (9/278). QGCS low score compared to the cervix was superior in sensitivity (83.3 % vs. 66.6%) for preterm delivery before 34 weeks, sensitivity 55.5% vs. 22.2%. The positive predictive value was 31.2% vs. 23.5% for delivery before 34 week and 31.2% vs. 11.7% for delivery between 34 and 37 weeks. The conclusion was that QGCS has the same if not better predictive value compared with shortened CL for prediction of preterm birth.

Finally, we conclude that we have through our results and the results of other authors in this study failed to show a clear connection between a shortened cervix with preterm birth. Accordingly, cervicometry seems to be one of the best methods available to us in the diagnosis and defining risk groups for preterm birth. In addition, infection as an etiological factor should not be neglected even independently of other screening methods as in our study, lack of association with infection and cervical insufficiency, and the combination of these two risk factors and clearly dominant becomes associated with preterm birth in both study groups.

6. CONCLUSION

The analysis of the first and second goal of our study we can conclude that ultrasound assessment of cervical length is simple and feasible in the 16th week of pregnancy in both groups, with high and low risk.

The length of the cervix in this period is shorter in the high risk group compared with the low-risk group. This difference was not statistically significant, however, it clearly demonstrated connection between shorter length of the cervix with the preterm birth.

A regression analysis shows that the shortening of the length of the cervix was larger in high risk group which is to be expected, bearing in mind that in this group, the risk of preterm delivery was significantly higher.

Microbiological analysis of cervicovaginal smear is also a very useful data for determining risk groups for preterm birth. Pregnant women with positive findings have much higher incidence of preterm birth than those with normal vaginal flora.

Most frequent was infection with *G. vaginalis*, as one of the dominant causes of bacterial vaginosis in which exist emphasizes risk due to bacterial vaginosis as a significant cause of premature birth. It is also important a connection between infections and

shortened cervix as a cause of preterm birth, but unfortunately these results was not possible to determine which of these two factors is more important, and was primarily present.

CONFLICT OF INTEREST: NONE DECLARED.

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