Eradication of Cervical Canal Colonization In Treatment Associated With Prophylactic Cervical Cerclage: The LOOK FURTHER Study

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Abstract

BACKGROUND: The perioperative management of the cervical cerclage procedure is not unified. Controlling microbiome cervical status does not affect obstetric outcomes in general population, but it can be beneficial in cervical insufficiency. Eliminating cervical pathogens in those patients may increase the effectiveness, resulting in prevention of miscarriage or preterm labor and delivery of a baby capable of normal development.

METHODS: Thirty five patients undergoing cervical cerclage at the 2nd Department of Obstetrics and Gynecology, Medical University of Warsaw, were included in the study. The procedure was performed only after receiving a negative culture from the cervical canal.

RESULTS: Thirty one (88.5%) patients delivered after the 34th and 28 (80%) after the 37th week of gestation. The colonization of genital tract was found in 31% of patients prior to the procedure, 42% in the subsequent course of pregnancy and 48% before delivery. Eighty five percent of patients who had miscarriage or delivered prematurely had abnormal cervical cultures. In patients with normal cervical cultures 91.67% women delivered at term. There were no abnormalities in children's development.

CONCLUSIONS: Controlling microbiological status of the cervical canal results in better or similar outcomes to those reported by other authors in terms of obstetric and neonatal outcomes. Active eradication of the reproductive tract colonization potentially increases the effectiveness of the cervical cerclage placement.

Plain English Summary

Cervical insufficiency is a common cause of recurring miscarriage in the second trimester. One of the main method of the prevention of recurrent pregnancy losses due to cervical insufficiency is cervical cerclage placement. The proceeding before and after the procedure is not yet unified.

In our study genital tract cultures were collected from all patients before the cervical cerclage procedure. If pathogens were detected, patients were treated according to the antibiogram and control cultures were collected two days after completion of therapy. After receiving a negative culture from the genital tract, the cervical cerclage placement was performed. Control swabs were collected from patients during follow-up every 2-3 weeks or when symptoms of genital infection occurred. Thirty five patients qualified for prophylactic or ultrasound-indicted cervical cerclage placement were included in the study. At least two years after birth, patients were asked by phone about their children's development.

In study population 80% of patients delivered after 37th week of gestation. Among patients with normal cervical cultures over 91% of women delivered at term. Eighty-five percent of patients who miscarried or delivered prematurely had abnormal cervical cultures during pregnancy. Ninety-one percent of children included in the study had no developmental abnormalities at the age of two.
In conclusion, controlling the results of cervical swabs and treatment of reproductive tract colonization is a promising method of improving obstetric outcomes in patients with prophylactic and ultrasound-indicated cervical cerclage.

1. Introduction

Preterm labor occurs in 10.6% of pregnancies and is the leading cause of children’s death before 5 years of age worldwide making it an obstetric challenge of great importance [1]. It occurs in cervical insufficiency which is a cervical inability to sustain pregnancy in the second trimester without clinical contractions, bleeding or preterm premature rupture of membranes (pPROM) [2]. In patients with a history of cervical insufficiency another preterm labor is more likely to occur than in patients with history of pPROM or spontaneous contractions in previous pregnancies [3]. One of the methods of its treatment is cervical cerclage placement both in women with symptomatic cervical insufficiency and as prophylaxis in patients with history of obstetric problems.

The current recommendations for the cervical cerclage procedure emphasize that perioperative antibiotic therapy does not affect obstetric outcomes [2]. These recommendations did not address the pregnancy management after this procedure. Perioperative and postoperative management varies considerably between maternal-fetal units. Although the effect of perioperative antibiotic therapy on the effectiveness of cervical cerclage has not yet been proven, this therapy is used in many departments [4]. Lindsay Wood and Owen reported that active cervicitis is a contraindication to cervical cerclage placement, while at the same time, these authors did not recommend routine diagnosis and treatment of colonization prior to surgery. According to the authors, such management does not affect obstetric outcomes. The articles cited by Lindsay Wood and Owen refer to the general population of pregnant women, not patients with cervical cerclage [5]. The authors have emphasized the role of the genital tract microbiome in obstetric failure [6, 7, 8]. They indicate that controlling the microbiological status of the cervix and eliminating pathogens in patients who require cervical cerclage placement may increase the effectiveness of this procedure. Perioperative and postoperative management of the cervical cerclage procedure may impact obstetric outcomes. A cervical cerclage is placed to prevent miscarriage or premature labor and to deliver a newborn baby capable of normal development. The purpose of our study was to present the obstetric, neonatal and pediatric outcomes of patients undergoing the cervical cerclage placement procedure in our obstetric department using a regimen of care that includes control of the microbiological status of the cervix and elimination of the pathogens detected.

2. Materials And Methods

The LOOK FURTHER study was a prospective observational study of patients at risk of preterm delivery in a group with potential cervical incompetence. The study covered thirty-five patients with singleton pregnancies undergoing either prophylactic cervical cerclage (PCC) or ultrasound-indicated cervical cerclage (UCC) at the 2nd Department of Obstetrics and Gynecology, Medical University of Warsaw. The study included every patient who underwent UCC or PCC procedure from January 2016 to December
2018. During the analyzed period, the patients underwent the same therapeutic procedure performed by the same experienced surgical team.

The inclusion criteria for the study were singleton pregnancy and placement of PCC or UCC. Indications for PCC placement included at least one late miscarriage (after the 15th week of gestation), a history of preterm delivery due to cervical incompetence, or placement of a cervical cerclage in a previous pregnancy. The indications for UCC were, according to ACOG recommendations, cervical length < 25 mm on transvaginal ultrasound performed before the 24th week of gestation, and history of preterm delivery before the 34th week. Cerclages were placed between the 12th and 23rd weeks of gestation. Due to similar obstetric outcomes in patients with PCC and UCC in the available literature [9, 10], these groups were combined. The exclusion criteria for the surgery were lethal fetal defects, intrauterine fetal death, genital tract bleeding, pPROM, uterine contractile function, and lack of patient consent for the procedure. Patients with emergency cerclage placement were not included in the analysis because in this group, while waiting for negative culture results, the risk of miscarriage increases significantly more than in the PCC and UCC groups; thus, the risk of patient selection bias increases.

Before the cervical cerclage placement procedure, cervical canal cultures were collected from all patients to test for aerobic bacteria, anaerobic bacteria, and fungi. Moreover attending physicians of two patients included in our research decided to additionally collect cervical canal cultures to test for atypical bacteria (Mycoplasma and Ureaplasma). The main purpose of collecting cervical swabs before PCC/UCC procedure was to provide sterile environment before the medical procedure in which we introduce a foreign body (cerclage) to the cervix. In addition it enables to avoid iatrogenic infections. If pathogens were detected, patients were treated according to the antibiogram. Two days after completion of antibiotic therapy, control cultures were collected. After receiving a negative culture from the cervical canal, the cervical cerclage placement procedure using the McDonald cerclage was performed [11]. Coated, braided polyester 2 Ti-Crone ™ sutures were used for the procedure. The procedure was performed under spinal anesthesia. Perioperatively, 3 doses of 1.5 g ampicillin with sulbactam were administered intravenously as antibiotic prophylaxis. Patients were discharged from the hospital with the recommendation of a bed rest and micronized progesterone sublingually at a dose of 300 mg daily (31 patients) or dydrogesterone orally at a dose of 30 mg daily (4 patients). During the follow-up, patients had cultures taken when a genital tract infection was suspected or follow-up cultures taken every 3–4 weeks. If a pathogen was detected in the cervical canal, treatment was ordered according to the antibiogram. No amniocentesis was performed to assess the microbiological status of the amniotic fluid.

Patients were admitted to the department if uterine contraction activity was present, bleeding from the birth canal happened, pPROM occurred, or signs of intrauterine infection were observed. All pregnant patients admitted to the department had cervical canal cultures taken upon admission. In the case of pPROM patients received empirical antibiotic therapy—cefuroxime intravenously (3 doses of 1.5 g per day for 7 days or until the antibiogram indicated insusceptibility, in which situation the antibiotic was changed according to the results). In cases of uterine contractions before the 36th week, patients received tocolysis with intravenous fenoterol or atosiban. Patients with threatened preterm labor up to the 36th
week of gestation received prenatal steroid therapy with betamethasone or dexamethasone at a total
dose of 24 mg intramuscularly. The cervical cerclage was removed in the case of intrauterine infection
signs, regular uterine contractions that were not reduced after tocolysis, bleeding from the genital tract or
electively at the 36−37th week of gestation. Cervical cerclages were not removed when pPROM occurred.
If cesarean section was performed, amniotic fluid culture was collected from each patient during the
operation.

Patient characteristics, obstetric history, perioperative, pregnancy, perinatal data, and neonatal outcomes
were obtained from medical histories. Detailed characteristics is presented in Table 1 and in the Appendix
Table S1. All children in Poland undergo 6 well-child visits before the age of 3 years. Such visits consist
of standardized clinical examination and assessment of child's development. In cases when the labor
was before 37 weeks of pregnancy the well-child visits are corrected for the estimated date of delivery. At
least two years after birth, patients were asked by phone about their children's development including
deviations in the two-year-old routine health check and whether children over 3 years of age were
attending kindergarten with their peers.

The main endpoint in the study was normal child development by at least 2 years of age. Additional
endpoints were created for comparison with other studies: prolonging the pregnancy to the 34th or 37th
week, miscarriage, intrauterine fetal death, neonatal death, or neonatal respiratory distress requiring
intervention. The authors refrained from analyzing cerclage latency as an endpoint because it is not
indicative of the procedure's effectiveness; the length of cerclage retention for prophylactic cerclage is not
directly related to pregnancy prolongation and largely depends on the week of pregnancy in which the
procedure was performed (Figure A).

Due to the small size of the group included in the study, with group size ratios and the assumption of an
odds ratio based on previous literature in the range of OR 1.1−2.0, in the analysis of risk factors for
therapeutic failure, we had the power of 4−10%. Therefore, it was decided to present the results
descriptively.

Comparison of the results obtained with those of other authors was performed using the Chi2 and
Fisher's tests in SAS 9.4 software.

3. Results

Thirty-five patients who underwent PCC placement (31 patients) or UCC placement (4 patients) were
included in the study. Maternal characteristic is presented in Table 1. Detailed patient outcomes are
presented in Appendix – Table S1.
Table 1
Patients’ characteristics.

| Variable                          | Patients with prophylactic cervical cerclage |
|-----------------------------------|---------------------------------------------|
|                                   | N (%)                                       |
| Age [years]                       |                                             |
| 20-29                             | 8 (22.86)                                   |
| 30-39                             | 22 (62.86)                                  |
| ≥40                               | 5 (14.29)                                   |
| Marital status                    |                                             |
| Unmarried                         | 7 (20)                                      |
| Married                           | 28 (80)                                     |
| Educational level                 |                                             |
| Elementary and technical college  | 2 (5.71)                                    |
| Secondary                         | 7 (20)                                      |
| Tertiary                          | 26 (74.29)                                  |
| Type of work                      |                                             |
| Physical                          | 6 (17.14)                                   |
| Intellectual                      | 27 (77.14)                                  |
| Unemployed                        | 2 (5.71)                                    |
| Place of residence                |                                             |
| Countryside                       | 4 (11.43)                                   |
| City <50 000 population           | 12 (34.29)                                  |
| City ≥50 000 population           | 19 (54.29)                                  |
| Pre-pregnancy BMI [kg/m²]         |                                             |
| 18.5 -24.9                        | 19 (54.29)                                  |
| 25-29.9                           | 9 (25.71)                                   |
| ≥30                               | 7 (20)                                      |
| History of vaginal delivery       |                                             |
| 1                                 | 15 (42.86)                                  |
| 2                                 | 8 (22.86)                                   |
| Variable                                      | Patients with prophylactic cervical cerclage N (%) |
|----------------------------------------------|---------------------------------------------------|
| History of cesarean section                  |                                                    |
| 1                                            | 7 (20)                                            |
| 2                                            | 2 (5.71)                                          |
| History of miscarriage                       |                                                    |
| 1                                            | 14 (40)                                           |
| 2                                            | 10 (28.57)                                        |
| ≥3                                           | 2 (5.71)                                          |
| History of preterm births [weeks of gestation] |                                                  |
| Delivery < 37 0/7                             | 18 (51.43)                                        |
| 22 0/7 – 26 6/7                              | 10 (28.57)                                        |
| 27 0/7 – 31 6/7                              | 3 (8.57)                                          |
| 32 0/7 -34 6/7                               | 5 (14.29)                                         |
| Cesarean section <37 0/7                     | 6 (17.14)                                         |
| 25 0/7 – 27 6/7                              | 4 (11.43)                                         |
| 29 0/7 -32 6/7                               | 2 (5.71)                                          |
| History of cervix injury                     |                                                    |
| Cervical conization                          | 3 (8.57)                                          |
| Mechanical dilatation                        | 11 (31.43)                                        |

Thirty-one (88.57%) patients delivered after the 34th week of gestation, and 28 (80%) carried the pregnancy for at least 37 weeks (Table 2 and Appendix – Table S1). We observed the following complications: 1 miscarriage, 1 neonatal death, 2 cases of chorioamnionitis, and 2 cases of pPROM.
Table 2
Outcomes of cervical cerclage procedure.

| Variable | Patients with cervical cerclage |
|----------|---------------------------------|
|          | N (%)                           |

| Gestational age at cervical cerclage performance [weeks of gestation] | |
|<16 0/7 | 13 (37.14) |
|≥16 0/7 | 22 (62.86) |

| Gestational age at delivery/miscarriage [weeks of gestation] | |
|< 22+0 | 1 (2.86) |
| 22+0 - 27+6 | 1 (2.86) |
| 28+0 - 33+6 | 2 (5.71) |
| 34+0 - 36+6 | 3 (8.57) |
| ≥37 | 28 (80) |

Of the patients included in the study, 17 gave birth naturally (1 patient by vacuum extraction), and 17 patients gave birth by cesarean section, of which 12 were performed intrapartum.

There were no complications related to cervical cerclage placement such as perioperative pPROM, spontaneous suture displacement, or cervical trauma complicated by genital tract bleeding. Prior to cervical cerclage placement, 11 (31.43%) patients were found to have colonization of the genital tract; in 5 (14.26%) of these patients, more than one microorganism was detected. In the subsequent course of pregnancy, abnormal cervical cultures were found in 15 (42.86%) patients, of which 9 (25.71%) had more than one microorganism. In the cervical canal cultures taken before delivery, pathological flora was found in 17 (48.57%) patients, of which 6 (17.14%) had more than one microorganism. The most common positive cultures bacteria was Escherichia coli, followed by Enterococcus spp. and Candida spp. A detailed description of the microorganisms present in the cultures of the patients included in the study is provided in Table 3 and Appendix – Table S1.
### Table 3
Prevalence of microorganisms isolated in patients with prophylactic cervical cerclage.

|                        | Initial N (%) | After procedure during pregnancy N (%) | After procedure before labor N (%) |
|------------------------|---------------|----------------------------------------|-----------------------------------|
| **Normal**             | 24 (68.57)    | 20 (57.14)                             | 18 (51.43)                        |
| **Abnormal**           | 11 (31.43)    | 15 (42.86)                             | 17 (48.57)                        |
| *Escherichia coli*     | 3 (8.57)      | 11 (31.43)                             | 10 (28.57)                        |
| **Group B Streptococcus** | 2 (5.71)   | 3 (8.57)                               | 2 (5.71)                          |
| *Enterococcus spp.*    | 2 (5.71)      | 5 (14.29)                              | 5 (14.29)                         |
| *Klebsiella spp.*      | 0             | 2 (5.71)                               | 2 (5.71)                          |
| **Anaerobes**          | 2 (5.71)      | 4 (11.43)                              | 1 (2.86)                          |
| **Fungi**              | 5 (14.29)     | 3 (8.57)                               | 2 (5.71)                          |
| **Others*              | 2 (5.71)      | 5 (14.29)                              | 2 (5.71)                          |
| **One microorganism**  | 6 (17.14)     | 6 (17.14)                              | 11 (31.43)                        |
| **Two microorganisms or more** | 5 (14.29) | 9 (25.71)                              | 6 (17.14)                        |

*Citrobacter, Morganella, Bacteroides, Prevotella

A total of 85.71% of patients (6 of 7 women) who had miscarriage or delivered prematurely (before completing the 37th week of gestation) had abnormal cultures later in the course of pregnancy: 1 patient lost her pregnancy in the 16th week during septic miscarriage; 1 patient (UCC) gave birth in the 25th week and, due to complications of prematurity, including E. coli sepsis, the newborn died; 1 patient (UCC) with pPROM in the 26th week of gestation underwent cesarean section in the 28th week of gestation due to threatening intrauterine infection; 1 patient gave birth in the 34th week due to pPROM; and 2 other patients gave birth in the 36th week (1 naturally and 1 by cesarean section during labor due to abnormal CTG tracings). Twelve patients had normal cervical cultures throughout the pregnancy, and in this group, all patients delivered after the 37th week of gestation, except 1 patient who underwent cesarean section at the 30th week of pregnancy. This patient was suspected of having an intrauterine infection at 30 weeks gestation based on clinical symptoms, despite normal cervical canal cultures before and after cervical cerclage placement. A culture of amniotic fluid collected during the cesarean section detected Enterococcus faecalis.

In 3 cases, the children required treatment in the Neonatal Intensive Care Unit (NICU); 1 of these children (2.86%) born in the 25th week died of congenital sepsis caused by E. coli, and 2 other children (5.71%) born in the 28th and 30th weeks required mechanical ventilation due to respiratory distress (Table 4).
Table 4: Neonatal outcomes of cervical cerclage procedure.

| Variable                                         | Patients with cervical cerclage |
|--------------------------------------------------|---------------------------------|
| Stillbirth                                       | 0                               |
| Intraventricular hemorrhage                      | 3 (8.57)                        |
| Infantile respiratory distress syndrome          | 5 (14.29)                       |
| Early onset infection of a newborn               | 3 (3.57)                        |
| Birth trauma *                                   | 4 (11.43)                       |
| Neonatal death                                   | 1 (2.86)                        |
| *clavicle fracture, cephalohematoma              |                                 |

Analysis of the children's development (excluding the miscarriage in the 16th week and neonatal death) between the ages of 2 and 4 years showed no abnormalities in any of the children at the two-year-old routine health check. All the children who reached the age of 3 went to kindergarten with their peers.

4. Discussion

A cervical cerclage success rate of 94% in our study suggests the validity of testing bacteriological cultures both before the procedure and in the subsequent course of pregnancy. Targeted antibiotic therapy allows for effective eradication of pathogens. The procedure used by our team to control the microbiological status of the cervical canal allowed us to obtain better or similar results to those reported by other authors [10, 12, 13, 14, 15] both in terms of maintenance of pregnancy up to the 34th and 37th weeks of gestation and neonatal outcomes (incidence of respiratory disorders requiring treatment at birth and neonatal deaths at birth). The evaluation of the children's development, which has not yet been done by any of the cited authors, allows us to assume that the adopted scheme of management yields more than satisfactory results.

Any pregnancy loss is a heavy burden on a woman. Lee's analysis shows that women with one lost pregnancy in the second trimester demonstrate rates of successful pregnancies after cervical cerclage placement in a subsequent pregnancy similar to those of women with a history of two lost pregnancies. This result justifies cerclage placement after the first pregnancy loss and is consistent with current recommendations. In the cited study, 74% delivered no earlier than in the 37th week [15].

A study by Chen describing the obstetric outcomes of patients after PCC and UCC placement reported a neonatal survival rate that was not significantly different from that obtained in our study (86.9% vs. 94.2% in our group) [10]. However, in our study group, significantly more patients continued pregnancy beyond 36 weeks (55% vs. 80%), which may implicate neonatal complications. In the cited study, cultures
were performed only in direction of Group B Streptococcus (GBS), and the choice of antibiotic therapy was dependent on the opinion of the treatment team. Among the patients included in the study preoperative cultures were taken from 48 pregnant women, of whom 12 had abnormal results.

Similar to our study, Moisidis-Tesch et al. demonstrated a wide variety of pathogens residing in the cervical canal before the cervical cerclage placement procedure. In the cited studies, bacteria were found in 53% of the samples collected [12]. Among the 45 pathogens detected, the predominant were Enterococci (31%) and E. coli (27%). In the study cited above, GBS, which is the bacterium most frequently detected in other studies, accounted for only 6.7% of detected bacteria, which indicates the futility of limiting the collected swabs to only this pathogen. In the case of discovering cervical colonization, the patients would receive treatment consistent with the antibiogram for at least 24–48 hours before the procedure. No cultures were obtained to assess the effectiveness of therapy, and no cultures were obtained later in pregnancy. The article does not provide information on fungal determination. In our study group, Candida spp. was the most common pathogen in cultures of patients before the procedure and the third most common pathogen in swabs taken later in pregnancy. Moisidis-Tesch et al. found that the only antibiotics to which all cultured pathogens show sensitivity are vancomycin and imipenem which are antibiotics reserved for severe infections. These drugs are not applicable in the treatment of fungal infections, which were probably not considered by the authors [12].

Based on our experience, it seems preferable to always collect cultures and select drugs according to the antibiogram. In the study by Wang [14], despite the application of broad-spectrum antibiotics for 5 days after cervical suture placement in a group of patients with prophylactic cerclage, statistically fewer women maintained their pregnancies to the 37th week in comparison with our patients (54.9% vs. 80%), while no significant differences were noted in the percentage of patients who maintained their pregnancies to the 34th week (72.9% vs. 88.6% in our group). In the prophylactic cerclage group described by Liu [15], using perioperative antibiotics without cervical swabs, 60% of patients delivered after the 37th week compared to 80% in our study, and 70% delivered by the 35th week compared to 85% in our study.

During the planning phase of our study the literature suggested that patients with PCC and UCC have similar obstetrical outcomes. Nevertheless it turned out that patients with UCC had worse obstetric outcomes than those with PCC – none of them delivered at term and the only neonatal death occurred in a patient with UCC. On account of that it may be beneficial to investigate these groups separately in the future.

Brown et al. [6] presented a hypothesis regarding the causes of cervical insufficiency. The first part assumes that the etiology of cervical insufficiency is mechanical “impairment” of the cervix. It seems to us that this group in our study could be represented by 12 patients with normal cervical canal cultures throughout whole pregnancy (before and after the cervical cerclage placement procedure). As many as 11 patients in this group delivered after the 37th week of gestation, despite a history of preterm labor and/or cervical insufficiency. The second part of the hypothesis implies an association between the occurrence of cervical insufficiency and chronic inflammation resulting from colonization of the reproductive tract. In our study, it was possible to distinguish a group of 10 other patients in whom, despite treatment of
genital tract colonization before the cervical suture placement procedure, colonization with subsequent pathogens was detected throughout the pregnancy. This group of patients demonstrated the highest rate of preterm deliveries. In our opinion, active eradication of microorganisms colonizing the cervix even during periconceptional care should result in better obstetric outcomes, but further research is needed to prove this thesis. When the patient is already pregnant, active monitoring of cervical cultures is an ad hoc measure, but is the best possible measure in the author's opinion. The Evidence Report, which included 48 studies analyzing the effect of treatment of asymptomatic bacterial vaginosis (BV) on the incidence of preterm labor, did not show an effect of such treatment on obstetric outcomes (delivery in the 37th week of gestation, pPROM, intrauterine deaths, neonatal mortality) in the group of pregnant patients without history of obstetric problems; however, the results are inconclusive for the group with a history of preterm labor [16]. In mothers, side effects of antibiotic therapy were more common after oral than vaginal administration, with mild side effects such as pruritus or diarrhea predominating in both routes [16]. Similarly, a Cochrane systematic review showed no benefit of treating BV in the general pregnant population, use of antibiotic therapy was associated with a lower risk of pPROM and low birth weight in patients with history of obstetric problems. Furthermore, antibiotic therapy administered before the 20th week of gestation in the general pregnant population correlated with a lower risk of delivery before the 37th week of gestation [17]. We believe that patients at risk of preterm delivery should receive more detailed monitoring of the cervical microbiome.

Romero's study from 2019 shows that most of pathogens found in the amniotic fluid (75%) are typical vagina commensals and in 62.5% of women with bacteria cultured from their amniotic fluid also had these bacteria present in their vagina. It indirectly proves that the most common way for pathogens to access the uterine cavity is by ascending from vagina. Collecting cervical canal cultures and treating the pathogens according to the antibiogram before as well as after PCC/ UCC procedure is a way of preventing the ascending intrauterine infection [18].

The available literature on cervical cerclage has not analyzed the endpoint of child development at 2 years of age, making it impossible to compare our results with those of other authors. Over the past 30 years, advances in medical technology in the field of neonatology have enabled a significant increase in the survival rate of premature babies, including extreme preterm infants. Studies of older children indicate that prematurity is an important cause of future complications in the form of neurological disorders. The incidence of cerebral palsy and other forms of cognitive impairment has remained similar despite increased survival rates [19]. In a study of a French cohort of several thousand premature children, the incidence rate of cerebral palsy at two years of age was 4.6% in a group of 3599 children analyzed after two years. However, as many as 50.2% of children born between the 24th and 26th week of gestation, 40.7% of those born between the 27th and 31st week of gestation, and 36.2% of those born between the 32nd and 34th week of gestation, had lower scores on a standardized test assessing normal development at 24 months of age (assessment of gross and fine motor skills, communication skills, problem solving skills and social skills, with the reservation that deaf, blind, and cerebral palsy patients were excluded from the analyses) [20]. In addition, research results show that children born prematurely
are more likely to develop chronic diseases, such as asthma, kidney disease, and hypertension [21, 22, 23].

The limitation of our study is the relatively small group of covered patients, which makes it impossible to perform univariate and multivariate analyses with sufficient power of the test. The study design we adopted allows us to realistically assess the outcomes of patients qualified for the PCC and UCC insertion procedure, given the low risk of miscarriage while awaiting culture results or antibiotic therapy. The authors are aware that there may be a small group of patients who, because of prolonged antibiotic therapy, enter a period of pregnancy in which a cervical cerclage can no longer be placed, but this does not mean that they do not benefit from preoperative management alone.

5. Conclusions

Our study indicates that active eradication of reproductive tract colonization is a promising method to potentially increase the effectiveness of the cervical cerclage placement procedure and the chance of normal child development. Taking cervical cultures in this small, selected group of patients is cost-prohibitive compared to potential benefits; the costs of treating preterm infants are much higher. The authors believe that neonatal and pediatric outcomes should be particularly considered when analyzing the efficacy of a procedure, as they represent the sole and overarching endpoint. The datasets supporting the conclusions of this article are included within the article and its Appendix.

List Of Abbreviations

pPROM - preterm premature rupture of membranes

PCC - prophylactic cervical cerclage

UCC - ultrasound-indicated cervical cerclage

BMI - body mass index

NICU - Neonatal Intensive Care Unit

GBS - Group B Streptococcus

BV - bacterial vaginosis

Declarations

Ethic Approval: The study was announced to the Medical University of Warsaw Bioethics Committee.

Consent to Participate: Not applicable.

Consent for Publication: Not applicable.
Availability of data and material: Data and material are included in Additional file 1. In case any more detailed information needed data and material are available to Corresponding Author.

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Figures
Figure 1

Time interval from cervical cerclage performance to delivery /miscarriage [days]

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