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Original Research Paper

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"PREGNANCY OUTCOME IN CERVICAL INCOMPETENCE: COMPARISON OF COMBINED USE OF CERCLAGE AND ORAL PROGESTERONE VERSES HIGH DOSE OF VAGINAL PROGESTERONE"

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ABSTRACT

INTRODUCTION- Cervical insufficiency, earlier known as cervical incompetence, is the inability of the cervix to maintain pregnancy till term due to structural or functional defects. Approximately 16.25% of second-trimester pregnancy losses and 2% of premature deliveries are due to cervical incompetence.

OBJECTIVE- The purpose of this study was to compare the outcome of pregnancy in patients who underwent early (12-16 weeks) cervical cerclage along with oral progesterone supplementation versus those having remedied with high dose intravaginal progesterone supplementation.

MATERIAL AND METHOD- This retrospective study was conducted in a maternity hospital in Gwalior from 1st January 2018 to 30th June 2021.

Comprehensive history, thorough clinical examination, laboratory investigations, ultrasonography measurement of cervical length, mode of delivery, gestational age at the time of delivery, neonatal outcome, NICU admission, and other parameters were collected from the medical files. patients were divided into two groups.

- Group 1(N-49) – Those who were remedied with high-dose vaginal progesterone supplementation continued uptil 34 wks of gestation.

Group 2 (N-49) – Those who underwent Mc Donald type of cervical encerclage at 12-16 weeks along with oral progesterone (10 mg Duphaston twice daily dose) supplementation continued up till 34 weeks of gestation.

RESULT- In our study, in the cervical cerclage group, only (4.1%) patients were delivered before 34 weeks while in the vaginal progesterone group (18.4%) patients were delivered before 34 weeks.

In the cervical cerclage group (53.1%) patients were delivered between 34-37 weeks while in the vaginal progesterone group, (44.9%) of the patient delivered between 34-37 weeks.

In the cervical cerclage group, the cesarean section rate was lower than only the vaginal progesterone group and admission to NICU of babies was also less (22.4%) in this group in comparison to the vaginal progesterone only group (36.7%).

CONCLUSION- Our study showed that cervical cerclage plus oral progesterone supplementation in women with extremely shortened cervix significantly decreased overall spontaneous preterm birth rates, prolonged pregnancy latency, and decreased the overall neonatal morbidity and mortality and is more effective than the vaginal progesterone group.

KEYWORDS : cervical incompetence, cerclage, progesterone supplementation

1. INTRODUCTION:

Cervical insufficiency, earlier known as cervical incompetence, is the inability of the cervix to maintain pregnancy till term due to structural or functional defect[1,2] cervical insufficiency results in a process of painless cervical dilation, leading to recurrent second-trimester pregnancy loss and preterm delivery in an otherwise normal pregnancy. [2.] The incidence of cervical insufficiency in the general obstetrics population is approximately 1:100 and 1:2000. Approximately 16.25% of second-trimester pregnancy losses and 2% of premature deliveries are due to cervical incompetence [3]. Cervical incompetence contributes to fetal loss and neonatal morbidity and mortality to a great extent. One of the biggest obstetric challenges is the diagnosis and management of a short cervix as multiple guidelines and definitions exist.[4] Cervical incompetence may be congenital or acquired. The most common congenital reason is a defect in the embryological development of Mullerian ducts.

In Ehlers-Danlos syndrome or Marfan syndrome, due to collagen deficiency, the cervix is not able to perform adequately, leading to its insufficiency. Acquired causes may include trauma to the cervix,(birth associated), forceful dilatation during MTP, cone biopsy, LEEP, cervical amputation, and others. Cervical insufficiency is rarely a marked and well-defined clinical entity but only part of a large and more complex spontaneous preterm birth syndrome. Cervical insufficiency usually transpires during the middle of the second or early third trimester.

However, in the majority of patients, cervical changes are the result of infection/inflammation, which causes early onset of the final pathway of parturition. Cervical insufficiency is a major cause of late miscarriage, and the diagnosis is often made retrospectively after a woman has had a second-trimester loss. Most of the women have no symptoms or only mild symptoms beginning in the early second trimester. These include abdominal cramping, backache, pelvic pressure, vaginal discharge which increases in volume, vaginal discharge which changes from clear to pink, and spotting.[4]

The diagnosis of cervical insufficiency is challenging because of the lack of objective findings and clear diagnostic criteria. Cervical ultrasound has emerged as a proven, clinically useful screening and diagnostic tool in the selected population of high-risk women based on an obstetrical history of a prior (early) spontaneous preterm birth. The transvaginal ultrasound typically shows a short cervical length, less than or equal to 25 mm, or funneling, ballooning of the membranes into a dilated internal os but with the closed external os.[5]

Many non-surgical and surgical modalities have been proposed to treat cervical insufficiency. Certain nonsurgical approaches, including activity restriction, bed rest, and pelvic rest have not proven effective in the treatment of cervical incompetence and their use is discouraged. Another nonsurgical treatment to be considered in patients at risk of

cervical insufficiency is the vaginal pessary. The evidence is limited for a potential benefit of pessary placement in select high-risk patients.

Three main interventions have been proposed to manage patients with a sonographic short cervix[6]

1. Vaginal progesterone administration
2. Cervical cerclage for patients with prior history of preterm birth
3. A vaginal pessary

Surgical approaches include transvaginal and transabdominal cervical cerclage. The two types of this commonly used vaginal procedure include McDonald's and the modified Shirodkar procedure. McDonald's technique involves taking four or five bites of number 2 monofilament suture as high as possible in the cervix, trying to avoid injury to the bladder or the rectum, with a placement of a knot anteriorly to facilitate the removal. The Shirodkar procedure involves the dissection of the vesical-cervical mucosa in an attempt to place the suture as close to the cervical internal os. The bladder and rectum are dissected from the cervix in a cephalad manner, the suture is placed and tied, and mucosa is replaced over the knot. Nonresorbable sutures should be used for cerclage placement using the Shirodkar procedure.

Absolute contraindication to cerclage operations is uterine contraction or labor (cervical dilatation >4cm), chorio amnionitis or vaginal infection, unexplained vaginal bleeding, rupture of membrane, intrauterine fetal death, Major congenital fetal anomaly.[7,8]

It has been observed that progesterone supplementation can result in a significant reduction of preterm birth and neonatal morbidity and mortality. Also, cervical cerclage has reduced the risk of preterm labor for a selected population of singleton pregnancies, those with a previous history of preterm birth and a shortened cervix.

A sonographic short cervix has emerged as a very powerful predictor of preterm birth.[8,9]

2. OBJECTIVE:

The purpose of this study was to compare the outcome of pregnancy in patients who underwent early (12-16 weeks) cervical cerclage along with oral progesterone supplementation versus those having remedied with high dose intravaginal progesterone supplementation alone in terms of:

- Gestational age at delivery
- Outcome- normal vaginal delivery/ LSCS
- Mean comparison of cervical length (cm)
- NICU admission and indications among the studied group

This retrospective study was conducted in a maternity hospital in Gwalior from 1st January 2018 to 30th June 2021.

INCLUSION CRITERIA:

- H/o repeated second-trimester abortions or preterm labor/ ultrasonographic diagnosis of the short cervix (<2.5cm)
- Early pregnancy period(12-16 weeks)
- Normal fetal scan or fetal anomaly ruled out

EXCLUSION CRITERIA:

- Patient is in active labor (cervical dilation > 4 cm)
- Significant infection or inflammation present (raised C-reactive protein or neutrophilia)
- Gestational age beyond 16 weeks
- Fetal anomaly detected in USG scan / fetal demise
- Ruptured membranes

Material And Method:

This is a retrospective study conducted extended from 1st January 2018 to 30th June 2021. Patients were divided into two groups.

Group 1(N-49) – Those who were remedied with high dose vaginal progesterone supplementation [(400 mg once daily vaginally (increased dose was given whenever required)] continued uptil 34 wks of gestation.

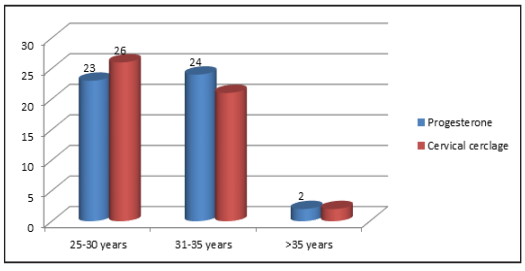
Group 2 (N-49) – Those who underwent Mc Donald type of cervical cerclage at 12-16 weeks along with oral progesterone (10 mg Duphaston twice daily dose) supplementation continued up till 34 weeks of gestation.

Comprehensive history, thorough clinical examination, complete blood count, fasting blood glucose, urine analysis, and culture ultrasonography measurement of cervical length, mode of delivery, gestational age at the time of delivery, neonatal outcome, NICU admission, and other parameters were collected from the medical files.

All the data were analyzed using IBM, SPSS Ver. 20 software. Cross Tabulation and frequency distribution were used to prepare tables. Data are expressed as numbers, percentages, and mean.

3. RESULTS:

Figure 1: Distribution of patients according to age in relation to two groups:



The above Figure shows the association between age distribution and Patient group.

The above association was found to be non-significant (p > 0.05) which shows the ages of patients of both groups are comparable. In **the Progesterone group (vaginal),** 23(46.9%) patients were in the age group 25-30 years, 24 (49.0%) patients were in the age group 31-35 years, 2(4.1%) patients were in the age group >35 years. In the **Cervical Cerclage group,** 26(53.1%) patients were in the age group 25-30 years, 21(42.9%) patients were in the age group 31-35 years, 2(4.1%) patients were in the age group >35years.

Table 2: Distribution of patients according to gestational age at delivery in relation to two groups:

Delivered at (Gestational Age/weeks)	Only Progesterone (High dose vaginal progesterone)		Cervical Cerclage (along with oral progesterone)		Total		P-value
	No.	%	No.	%	No.	%	.081
<34weeks	9	18.4%	2	4.1%	11	11.2 %	
34-37weeks	22	44.9%	25	53.1%	48	49.0%	
>37weeks	18	36.7%	21	42.9%	39	39.8%	
Total	49	100.0%	49	100.0%	98	100.0%	

The above table shows the association between gestational age and patient group.

The above association was found to be non-significant (p >0.05) which shows the gestational age at the time of delivery of patients of both groups are comparable. In **the progesterone group (vaginal),** 9(18.4%) patients were delivered in <34 weeks of gestation age, 22(44.9%) patients were 34-37 weeks of gestation age, 18(36.7%) patients were >37 weeks of gestation age. In the **cervical cerclage group,** 2(4.1%) patients were <34 weeks of gestation age, 25(53.1%) patients were 34-37 weeks of gestation age, 21(42.9%) patients were >37 weeks of gestation age.

Table 3: Distribution of patients according to the mode of delivery in relation to two groups:

Delivered at (Gestational Age/weeks)	Only Progesterone (High dose vaginal progesterone)		Cervical Cerclage (along with oral progesterone)		Total		P-value
	No.	%	No.	%	No.	%	<0.05
Normal Delivery	29	59.1%	32	65.3%	61	62.2%	
LSCS	20	40.8%	17	34.7%	37	37.7%	
-Elective	7	14.2%	8	16.3%	15	15.3%	
-Emergency	13	26.5%	9	18.3%	22	22.4%	
Total	49	100.0%	49	100.0%	98	100.0%	

The above table shows the comparison of Mode of Delivery between the two groups.

There was a statistically significant association seen between the mode of delivery and the groups (P<0.05). In the **Progesterone group,** 29 (59.1%) patients were normally delivered (vaginal) and 20 (40.8%) patients were delivered by LSCS. In the **Cervical Cerclage group,** 32 (65.3%) patients were delivered normally (vaginal) and, 17(34.7%) patients were delivered by LSCS.

Table 4: Comparison of admission to NICU between the two groups:

Admission to NICU	Only Progesterone (High dose vaginal progesterone)		Cervical Cerclage (along with oral progesterone)		Total		P value
	No.	%	No.	%	No.	%	.184
No	31	63.3%	38	77.6%	69	70.4%	
Yes	18	36.7%	11	22.4%	29	29.6%	
Total	49	100.0%	49	100.0%	98	100.0%	

The above table shows the association between Admission to NICU and Patient group.

The above association was found to be non-significant (p > 0.05) which shows the admission to NICU of babies of both groups are comparable. In **the Progesterone group (vaginal),** 18 (36.7%) babies were Admission to NICU. In the **Cervical Cerclage group,** 11(22.4%) babies were admitted to NICU.

4. DISCUSSION:

The placement of a cervical cerclage appears to be indicated in patients having acute cervical insufficiency and in some patients with a prior history of PTB and a cervix less than 25mm. Thus there are two major interventions that may reduce the rate of preterm delivery in patients with a prior history of PTB and a cervix less than 25 mm; vaginal progesterone administration and cervical cerclage.[4,5]

In this study, we have compared two groups of patients. In one group only high dose vaginal progesterone was administered and in another group cervical cerclage was supplemented with oral progesterone.

The association between the age group of the patients and treatment modalities given to them was found to be non-significant (p > 0.05) which shows the ages of patients of both groups are comparable. In **the Progesterone group (vaginal),** 23(46.9%) patients were in the age group 25-30 years, 24 (49.0%) patients were in the age group 31-35 years, 2(4.1%) patients were in the age group >35 years. In the **Cervical Cerclage group,** 26(53.1%) patients were in the age group 25-30 years, 21(42.9%) patients were in the age group 31-35 years, 2(4.1%) patients were in the age group >35years.

The gestational age in both groups was found to be non-significant (p >0.05) which shows the Gestational age (at time of delivery) of patients of both groups are comparable. In **the Progesterone group (vaginal),** 9(18.4%) patients were <34 weeks of gestation age, 22(44.9%) patients were 34-37 weeks of gestation age, 18(36.7%) patients were >37 weeks of gestation age. In **the cervical cerclage group,** 2(4.1%) patients were <34 weeks of gestation age, 25(53.1%) patients were 34-37 weeks of gestation age, 21(42.9%) patients were >37 weeks of gestation age.

There was a statistically significant association seen between the mode of delivery and the groups (P<0.05). In **the Progesterone group,** 29 (59.1%) patients were normally delivered (vaginal) and 20 (40.8%) patients were delivered by LSCS. In **the Cervical Cerclage group,** 32 (65.3%) patients were delivered normally (vaginal) and, 17(34.7%) patients were delivered by LSCS.

Admission to NICU was found to be non-significant (p > 0.05) in our study which shows the admission to NICU of babies of both groups are comparable. In **the Progesterone group (vaginal),** 18 (36.7%) babies were admitted to NICU. In the **Cervical Cerclage group,** 11(22.4%) babies were admitted to NICU.

Agudelo AC et al (2013)[10] in their review concluded that in women with a sonographically short cervix in the mid-trimester, singleton gestation, and previous spontaneous preterm birth, vaginal progesterone administration was associated with a significant 53% reduction in the risk of PTB at <32 weeks, 57% decrease in perinatal morbidity and mortality and lesser admission to NICU. A cervical cerclage showed a significant 34% reduction in preterm birth and a 36% decrease in perinatal morbidity and mortality.

According to them if cerclage and oral progesterone were administered together, their efficacy was more. This finding is in accordance with our study.

Hassan HH et al (2011)[11] compared the incidence of preterm birth, perinatal morbidity, and mortality, admission to NICU, maternal complications in women with short CL receiving progesterone, and placebo treatment. They concluded that women receiving progesterone are less likely to suffer adverse effects as compared to women receiving placebo treatment. Our results are similar to them in a way that the use of progesterone may help in reducing preterm birth.

Kronemyer B (2019)[12] did a study on 286 pregnant women to compare the outcome of pregnancy in women with a short cervical length (≤ 25 mm) who were managed by one of four different treatment protocols: vaginal progesterone, cervical cerclage, and an Arabin cervical pessary (group A); Arabian cervical pessary and vaginal progesterone (group B); cervical cerclage and vaginal progesterone (group C); or vaginal progesterone alone (group D).

This finding suggests that a combined rescue therapy may have a synergistic effect in preventing preterm birth (PTB) in pregnant women with short cervical length and a high risk of

PTB, as well as perhaps extending pregnancy and safely bringing these pregnancies to near term. These results are similar to the outcome of our study.

Dang VQ et al (2020)[13] chose to compare two interventions directly to each other. Their data suggested that any of the two treatments (vaginal progesterone or cerclage) could reduce the risk of PTB and subsequent poor neonatal outcomes. The synergistic effect of both is more efficacious in treating short cervix. These findings can be easily correlated to our study where the group which received cerclage with progesterone was better than the group which received only progesterone.

5. CONCLUSION:

Vaginal progesterone and cervical encerclage are not equally effective for the prevention of preterm birth in women with singleton pregnancies, previous preterm birth, and short cervix. Our study showed that cervical encerclage plus oral progesterone supplementation, significantly decreased overall spontaneous preterm birth rates, prolonged pregnancy latency, and decreased the overall neonatal morbidity and mortality, and is more effective than the vaginal progesterone group.

Further investigation and confirmation of this finding in a larger prospective trial are warranted to explore this potential benefit for the prevention of preterm birth in the future in patients with a short cervix.

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