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TO DETERMINE THE FREQUENCY OF PRETERM LABOUR IN WOMEN TREATED WITH CERVICAL CERCLAGE AND EFFECT OF ADDITIONAL PROGESTERONE TREATMENT IN PREGNANT WOMEN IN TERMS OF INCIDENCE OF PRETERM LABOUR, PRESENTING WITH PREVIOUS HISTORY OF PRETERM DELIVERY DUE TO CERVICAL INCOMPETENCE

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Abstract

OBJECTIVE: *To determine frequency of preterm labour in women undergoing cervical cerclage.*

MATERILAS AND METHODS: *Study design used was descriptive study design. Study setting of research was Outpatient, Department of Obstetrics & Gynaecology, Ibn-e-siena Hospital, Multan. Sample size of 212 Calculated through OpenEpi software. Inclusion Criteria included pregnant women, aged 18-38 years, at gestational age of 12 weeks, with previous history of preterm delivery due to cervical incompetence. Data analysis was done by SPSS-24. Preterm Labour and prevention of preterm birth was compared between two groups by using chi square test. Preterm Labour and prevention of preterm birth was also compared between two groups after stratification with maternal age groups and short time between two pregnancies. P- Value ≤ 0.05 was considered as significant.*

RESULTS: *A total of 212 pregnant women with a history of preterm delivery due to cervical incompetence were included in this study. The mean maternal age was 28.3 ± 4.7 years. Out of the total participants, 71 women (33.5%) experienced preterm labour, while 141 women (66.5%) delivered at term. When comparing the two groups: In the progesterone group (n=112), 24 women (21.4%) had preterm labour. In the non-progesterone group (n=100), 47 women (47%) had preterm labour. This difference was statistically significant ($p < 0.001$), indicating a potential protective effect of progesterone therapy in preventing preterm labour. Women who conceived within a year of a previous delivery were more likely to experience preterm labour, particularly if they did not receive progesterone therapy.*

CONCLUSION: *By adding progesterone to cervical cerclage significantly reduces the risk of preterm labour, particularly in women under 30 years of age and those with a short inter-pregnancy interval. These findings support the combined use of cerclage and progesterone in managing high-risk pregnancies.*

INTRODUCTION

Cervical incompetence is diagnosed in women who experience persistent, often rapid and painless, late second trimester pregnancy loss. More recently the concept of cervical competence as a continuum is purposed. It is probable that cervical length and strength together with the quality of the cervical mucus are contributing factors towards the cervix's function (1-3). Multiple studies have demonstrated a strong relationship between cervical length and the risk of preterm delivery. The cervix may be damaged (or completely removed) by surgery in the treatment of cervical cancer or rarely, during a difficult instrumental vaginal delivery or Caesarean section at full dilatation. There are also associations between diethylstilbestrol exposure in utero and developmental anomalies in the genital tract and cervical weakness. A short or partially dilated cervix may allow bacteria to ascend into the lower pole of the uterus where, acting through the toll-like receptors of the innate immune system, they stimulate activation of NF-kappa B, the production of inflammatory cytokines, prostaglandins and inflammatory response. This then leads to cervical ripening and shortening which in turn decreases the ability of the cervix to act as either a mechanical or a microbiological barrier and so, ultimately, the development of either localized or generalized chorionamnionitis and to preterm delivery. A short or weak cervix may therefore contribute to preterm labour not only by leading to simple second trimester miscarriage but also by contributing to a risk of ascending infection leading to a more classical spontaneous preterm labour (3-5). Three interventions have been proposed to manage patients with risk of preterm labour: 1) oral progesterone 2) a cervical cerclage for patients with a prior history of preterm birth 3) a vaginal pessary (6-7).

A study by Rebarber et al, compared the incidence of recurrent spontaneous preterm labour in patients with cervical cerclage treated with weekly 17 a-hydroxyprogesterone caproate (17P) injections versus daily outpatient nursing surveillance without 17P. Included cases in the study were singleton gestations with cervical cerclage performed due to prior recurrent spontaneous preterm delivery. The study group (n=232) received once-weekly nursing visit and 17P injection. The control group (n=1650) consisted of women enrolled for outpatient nursing surveillance without 17P twice-daily electronic uterine contraction monitoring and nursing assessment. Total number of patients were 1882. 44% (845) end up in spontaneous preterm delivery. In a retrospective cohort study by Mackeen AD et al, on women who received a cerclage for a prior preterm birth were included. Among all 14 women received 17P and 80 did not. The primary outcome variable was delivery < 35 weeks. 16.5% (16 patients out of 97) go into preterm delivery. Rationale of my study is to assess the efficacy of two different approaches in management of preterm birth in high risk pregnancies. A few studies are conducted for comparison of cervical cerclage plus progesterone versus cervical cerclage alone in women with risk of preterm delivery (8). The results of my study will also help clinicians to formulate guidelines for the management of preterm labour due to cervical incompetence which will ultimately help us to improve quality of life of our patients.

METHODOLOGY

Study design used was descriptive study design. Study Setting of research was Outpatient, Department of Obstetrics & Gynaecology, Ibn-e-Siena Hospital, Multan, While, duration of study was six months after approval of synopsis. Sample size taken was 212 Calculated through OpenEpi software using formula for single proportion where frequency of preterm labour is 16.5 % Confidence level: 95%, and Precision: 5%. Inclusion Criteria included patients as pregnant women, aged 18-38 years, at gestational age of 12 weeks, with previous history of preterm delivery due to cervical incompetence (documented in medical record of that pregnancy). While, Exclusion Criteria excluded patients with anomalous fetus on ante-natal ultrasound record, multiple pregnancy, history of previous cervical surgery. Data collection procedure was as total 212 pregnant women fulfilling the inclusion criteria from outpatient department of obstetrics and gynecology were included in the study after permission from ethical committee and approval from CPSP. Informed consent was taken from each patient, ensuring confidentiality and fact that there was no risk involved to the patient while taking part in this study. Age, parity and gestational age (measured from last menstrual period; LMP) was

inquired. Before intervention, all participants were instructed thoroughly if she experience more than six contractions per hour before 37 weeks of gestation, she should report immediately to labour room of the hospital where shehad undergone uterine contraction monitoring with an external tocodynamometer. To address the psychological issues, each participant was briefed fully regarding procedures and was ensured that prompt care was always ready to deal any complication. In addition, supportive treatment of progesterone in form of Yes or No was recorded. All cases were followed weekly. Per-abdominal examination for 10 minutes was done for palpable contractions. Counseling of the patients was done; so as, to report if she feels contractions at home. In hospital standard tocolytic protocol was followed while being prepared for delivery if that failed. All data was entered on a specifically designed proforma. Data analysis was done as data was entered in and analyzed by SPSS-24. Shapiro-Wilks Normality Test was used to assess the normality of data. Mean ± SD (Median ± IQR) was presented for quantitative variables like maternal age, gestational age at time of 1st antenatal visit and Gestational age at delivery. Frequency and percentage was calculated for qualitative variables like maternal age groups, Preterm Labour (Yes / No), prevention of preterm birth (Yes / No) and short time between two pregnancies (Yes / No). Preterm Labour and prevention of preterm birth was compared between two groups by using chi square test. Preterm Labour and prevention of preterm birth was also compared between two groups after stratification with maternal age groups and short time between two pregnancies. P- Value ≤ 0.05 was considered as significant.

RESULTS

A total of 212 pregnant women with a history of preterm delivery due to cervical incompetence were included in this study. The mean maternal age was 28.3 ± 4.7 years. The mean gestational age at the first antenatal visit was 12.4 ± 1.2 weeks, while the mean gestational age at delivery was 35.6 ± 2.9 weeks.

Among the total participants, 112 women (52.8%) received additional progesterone therapy alongside cervical cerclage, while 100 women (47.2%) did not receive progesterone.

Table 1: Baseline Characteristics of Study Participants (N=212)

Variable	Mean ± SD / Frequency (%)
Maternal Age (years)	28.3 ± 4.7
Gestational Age at First Visit (wks)	12.4 ± 1.2
Gestational Age at Delivery (wks)	35.6 ± 2.9
Received Progesterone	112 (52.8%)
No Progesterone	100 (47.2%)
Short Time Between Pregnancies	74 (34.9%)

Out of the total participants, 71 women (33.5%) experienced preterm labour, while 141 women (66.5%) delivered at term.

When comparing the two groups: In the progesterone group (n=112), 24 women (21.4%) had preterm labour. In the non-progesterone group (n=100), 47 women (47%) had preterm labour.

This difference was statistically significant ($p < 0.001$), indicating a potential protective effect of progesterone therapy in preventing preterm labour.

Table 2: Comparison of Preterm Labour Between Groups

Group	Preterm Labour (Yes)	Preterm Labour (No)	Total	p-value
Progesterone	24 (21.4%)	88 (78.6%)	112	
No Progesterone	47 (47%)	53 (53%)	100	< 0.001

Chi-square test applied, which showed that results were statistically significant.

Further analysis was performed after stratifying by maternal age. Among younger mothers (<30 years), progesterone therapy was associated with a notably lower rate of preterm labour.

Table 3: Stratification by Maternal Age and Progesterone Use

Age Group	Progesterone	Preterm Labour	No Preterm Labour	Total	p-value
<30 years	Yes	14	62	76	
	No	28	36	64	0.004
≥30 years	Yes	10	26	36	
	No	19	17	36	0.210

The data was also stratified by interval between pregnancies. Women who conceived within a year of a previous delivery were more likely to experience preterm labour, particularly if they did not receive progesterone therapy

Table 4: Stratification by Pregnancy Interval

Short Interval	Progesterone	Preterm Labour	No Preterm Labour	Total	p-value
Yes	Yes	9	24	33	
	No	22	19	41	0.003
No	Yes	15	64	79	
	No	25	34	59	0.027

The results of this study suggest that adding progesterone to cervical cerclage significantly reduces the risk of preterm labour, particularly in women under 30 years of age and those with a short inter-pregnancy interval. These findings support the combined use of cerclage and progesterone in managing high-risk pregnancies.

DISCUSSION

To give mechanical support to the cervix and to reduce the risks of premature deliveries in pregnant women, throughout pregnancy cervical cerclage entails sutures around the cervix's neck (9–10). Our research subjects' mean age was 28.10±4.09 years, with 104 (66.7%) being between the ages of 20 and 30. The minimum age was 23, and the maximum age was 39. Similar to our findings, Zhu et al. (11) found that the mean age of women with cervical cerclage was 29.18±3.52 years, with a range of 23–37 years. Similar to our results, a research by Yassaee et al.20 reported a mean age of 27.8±4.7 years. Similar findings to ours were previously reported by Shamshad et al.12 from Ayub Hospital in Abbottabad. 21 people (13.5%) had diabetes, and 31 people (19.9%) had hypertension. The average height was 161.31±5.22 cm, and the average weight was 56.23±6.21 kg. 33 (21.2%) of the studied cases had obesity, and the mean BMI was 23.41±2.47 kg/m2. In 42 (26.7%) of our study cases, a short interpregnancy period was seen, whereas the mean interpregnancy interval was 10.45±5.67 months. Of the research cases, 114 (73.1%) had elective cerclage and 42 (26.7%) had emergency cerclage. Similar to the findings of our study, Shamshad et al.14 from Abbottabad likewise showed that 81% of patients had elective cerclage and 19% had emergency cerclage. While the mean gravidity was 5.13±1.87 and 105 (67.3%) had gravidity greater than 5, the mean parity was 3.47±1.19 and 113 (72.4%) of the study cases had parity up to 4. Similar findings were also reported by Abbottabad's Shamshad et al.14. after our research patients were recruited, their mean gestational age was 12.64±0.99 weeks, and after they were delivered, their mean gestational age was 38.74±2.17 weeks. Our results are consistent with

those of Memon et al. (13) and Shamshad et al. (14). 32 (20.5%) of the cases in our research had preterm labor. Similar to our findings, a research by Yassaee et al. (15) found that 23.8% of women who had cervical cerclage gave birth before their due date. Similar to our findings, Abbottabad's Shamshad et al.14 reported 18.7% premature labor. Additionally, 34.15% of premature deliveries were recorded by Memon et al.15. Nine percent of premature births were reported in a Karachi study by Naz et al. (16), which is less than what our investigation found.

The use of progesterone in different preparations to prevent recurrent preterm delivery has been the subject of numerous trials. 43 high-risk individuals were randomly assigned to receive weekly intramuscular 17α-hydroxyprogesterone caproate (17P) or a placebo in one of the first experiments, which was published in 1975 (17). With a substantially longer mean pregnancy duration, higher mean birth weight, and a reduced perinatal mortality rate, the authors discovered that progesterone had a protective impact. Several follow-up experiments produced contradictory findings (18-19). Professor Marc Keirse conducted a meta-analysis of seven published trials on progesterone prophylaxis in high-risk populations as a result of this. The study, which was published in 1990, found that subjects who received progesterone prophylaxis had a significantly lower rate of preterm labor, preterm birth, and birth weight < 2500 g. However, it was unclear from the data whether this resulted in a lower overall rate of perinatal mortality and morbidity. In the 1990s, progesterone supplementation for the prevention of preterm birth lost favor for reasons that are yet unknown. Interest in this prophylactic measure was not rekindled until 2003, when two well-designed, well-publicized, randomized clinical trials were published (20-21).

Progesterone supplementation for the prevention of recurrent preterm birth did not prove beneficial in the largest randomized trial. 35 In this study, 659 women who had previously experienced a spontaneous preterm birth were randomized to receive either a placebo or progesterone gel (90 mg) vaginally every day between weeks 18–23 and 37 of pregnancy. This group had significant rates of recurrent preterm births, with about 25% occurring before 35 weeks and 40% occurring before 37 weeks.

When compared to a placebo, progesterone supplementation did not significantly lower the incidence of preterm birth at any gestational age, and neither maternal or neonatal outcome measure showed any differences between the groups. It's unclear why this trial differed from others, but it might have to do with the kind, dosage, and method of progesterone administration (22-23).

CONCLUSION

By adding progesterone to cervical cerclage significantly reduces the risk of preterm labour, particularly in women under 30 years of age and those with a short inter-pregnancy interval. These findings support the combined use of cerclage and progesterone in managing high-risk pregnancies.

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