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C-Reactive Protein and White Blood Cell Count at Pre / Post Cervical Cerclage Predict Early Preterm Labour

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ABSTRACT

Background and Aim: Preterm birth affects over 15 million infants annually worldwide, with cervical insufficiency being a major contributing factor. This study evaluates CRP and WBC levels in pregnant women undergoing cervical cerclage to predict Early Preterm Birth (EPTB) risk.

Methods: A prospective observational study conducted at Bint al-Huda Hospital, Thi-Qar, Iraq, from December 2023 to December 2024. Fifty-four pregnant women with singleton pregnancies and cervical insufficiency (cervical length <25 mm) were enrolled. CRP and WBC levels were measured pre-cerclage and on days 1 and 2 post-cerclage, with follow-up until delivery.

Results: Mean participant age was 30.2 years. Cervical length improved from 20.6 mm pre-cerclage to 23.8 mm post-cerclage. Mean gestational age at cerclage was 20.6 weeks, with delivery occurring at a mean of 35.3 weeks. Only 18.5% delivered before 34 weeks, while 81.5% delivered at or beyond 34 weeks. Elevated pre-cerclage CRP and WBC levels were significantly associated with increased EPTB risk. Post-cerclage monitoring identified persistent inflammation correlating with adverse outcomes.

Conclusions: CRP and WBC are reliable biomarkers for predicting EPTB in women undergoing cervical cerclage. Elevated pre-cerclage levels indicate higher risk, necessitating close monitoring and early intervention. Post-cerclage trends provide critical insights into inflammatory responses, enabling targeted management to improve maternal and neonatal outcomes. Further research is recommended to refine predictive models and explore therapeutic strategies.

Keywords: CRP, Cervical, Preterm Labour, WBC, Cervical Cerclage.

1. Introduction

Preterm birth refers to a birth that occurs before 37 weeks' gestation. It may be further classified as early and late preterm birth. Early preterm birth refers to the birth of a baby before 33 weeks of gestation, whereas late preterm birth refers to the birth of a baby between 34 and 36 weeks of gestation 1]. An estimated 15 million premature babies were born in 2013, more than one in ten infants born worldwide—before their due date. Out of them, one million children under the age of five die every year due to complications associated with premature delivery [2].

Measuring Early Preterm Birth and severe preterm birth in developing countries is very challenging, and the death rate is quite high [3]. The prevalence of preterm birth varies across Arab countries. In Iraq, a retrospective analysis conducted in Baghdad from November 2022 to January 2023 reported a prevalence of 7.5% among neonates admitted to the Neonatal Intensive Care Unit (NICU). The study included 115 preterm neonates, with 55% being male. Extremely preterm neonates (born before 28 weeks of gestation) comprised 6.1% of the cohort, while very preterm neonates (28 to <32 weeks) accounted for 30.4% [4]. The retrospective study in Baghdad reported an overall mortality rate of 6.9% among preterm neonates, with male infants accounting for 53% of these deaths. Survival rates at discharge varied between 50% and 95.8%, depending on gestational age [4]. In Saudi Arabia, a systematic review and meta-analysis encompassing 50,514 participants found a pooled prevalence of preterm birth of 7.89 per 100 live births [5].

Several studies have identified various risk factors contributing to preterm birth in Arab countries. In Iraq, a case-control study highlighted low socioeconomic status, hard work, urinary tract infections, and adverse obstetric histories as significant contributors to preterm labor and preterm pre-labor rupture of membranes [6]. In the United Arab Emirates, research indicated that Arab mothers were twice as likely to deliver preterm babies compared to non-Arab mothers.

Additionally, mothers with education levels below secondary school had a fourfold higher risk of preterm delivery. The study also found a strong association between preterm birth and low birth weight, with preterm infants being 18 times more likely to have low birth weight [7]. A study in Qatar identified advanced maternal age, pre-gestational diabetes mellitus, assisted pregnancies, and a history of preterm births as independent predictors for both preterm and early term births [8]. This study aims to evaluate the levels of CRP and WBC counts in pregnant women undergoing cervical cerclage to predict the risk of EPTB effectively.

2. Material and Methods:

2.1. Study Setting

It is a prospective observational study to assess the level of C-reactive protein and white blood cell count in pre and post cervical cerclage to predict Early Preterm Birth.

The study was conducted at the obstetrical ward at Bint al-Huda Hospital in Thi-Qar City during the period from December 2023 to December 2024.

2.2. Study population

Fifty-four pregnant women who presented with cervical cerclage indicated for short cervix at Bint al-Huda Hospital during the study period were included, informed consent was tacken. Then women were followed up till delivery.

2.3. Inclusion criteria

Women with a single pregnancy who had a short cervix (defined as less than 25 mm in length) detected by ultrasound and women who had a previous miscarriage in early second trimester were enrolled into the study.

2.4. Exclusion criteria

The exclusion criteria for women included women with visible or bulging fetal membranes into the vagina, multiple gestations, fetal anomalies or chromosomal anomalies, vaginal bleeding, spontaneous rupture of membranes, clinical suspicion of chorioamnionitis, and women with chronic medical

conditions such as diabetes mellitus, connective tissue disease and immunocompromised states.

2.5. Study tools

A questionnaire form was designed for the study which consisted of the following items: socio-demographic data such as age, educational background and profession. Past medical and surgical history in addition to medication history were collected. Women's height and weight were measured and body mass index (BMI) was calculated as: weight (kg) / height (m^2).

Pelvic sonography (transvaginal or transabdominal) was performed to measure cervical length and rule out multiple pregnancies. Blood was drawn from each participant and maternal serum CRP and WBC count were measured three times: before cerclage placement, 24 hours after cerclage placement and 48 hours after cerclage placement. Cerclage was performed using general anaesthesia. Prophylactic tocolytics were not given after the cerclage. Cerclage sutures were usually removed at 37 weeks' gestation in the absence of complications.

In patients with preterm labor, preterm rupture of membranes, or chorioamnionitis, cervical cerclage sutures were removed sooner. Post-cerclage cervical length was measured by ultrasonography. The patients were evaluated until delivery, and the gestational age at delivery, mode of delivery and neonatal outcome were noted. All women gave their informed consent and confidentiality was maintained.

2.6. Statistical Analysis

A computerized statistical program called the Statistical Package for Social Sciences (SPSS) version 26 was used to enter and analyze the data. The proper statistical tests were conducted: two samples independent t-tests were used for the continuous variable, and a Chi-square test was used for categorical variables. The significance threshold (p-value) is set at ≤ 0.05 for all statistical analyses.

3. RESULTS

The study included 54 women who underwent cervical cerclage. Their mean age was 30.2 years. 66.7% of them were housewives, 55.6% living in urban areas. 51.9% of women were illiterate and 11.1% of them had a college and higher education. All these data are presented in Table 1.

Table 1. The sociodemographic characteristics of participants

Characteristics	Levels	Number	Percentage
Age	Mean ± SD	30.2± 5.0	
	20-29	20	37.0
	30-39	32	59.3
	40	2	3.7
Occupation	Housewives	36	66.7
	Employer	18	33.3
Residency	Rural	24	44.4
	Urban	30	55.6
Education	Illiterate	28	51.9

	Primary	6	11.1
	Secondary	14	25.9
	College and higher education	6	11.1
Total		54	100.0

Table 2 shows the clinical variable among participants. 62.9% of the women mentioned that they had an adequate ANC. Regarding parity, 70.4% of women have 1-4 children.

Table 2. The clinical variables among participants

Variables	Levels	Number	Percentage
ANC	Adequate	34	62.9
	Inadequate	20	37.1
Parity	Nullipara	8	14.8
	1-4	38	70.4
	>5	8	14.8

Table 3 shows the current pregnancy characteristics. The cervical length mean is 20.6 mm among participants before cerclage and the mean increased to 23.8 mm post cerclage. Regarding the gestational age at which cervical cerclage was done at 20.6 weeks. While the mean gestational age of delivery among participants was 35.3 weeks. 18.5% of the participants had early premature labour.

The women's anthropometric characteristics are presented in Table 4. Their mean weight was 76 kg, and their mean height was 157.8 Cm. The mean BMI was 31.8. The majority of participants (72.2%) were overweight.

Table 3. The current pregnancy characteristics

Variables		Number	Percentage
Cervical length at cerclage	Mean ± SD	20.6± 2.7	
Cervical length post cerclage	Mean ± SD	23.8±3.4	
GA at the time of cerclage	Mean ± SD	20.6±1.7	
GA of delivery	Mean ± SD	35.3±4.3	
	weeks 34 >	10	18.5
	weeks 34 ≤	44	81.5

Table 4. The anthropometric characteristics

Percentage		Number	Variables
BMI	Mean ± SD	31.0±4.4	
	Normal	7.4	4
	Overweight	72.2	39
	Obese	20.4	11

The laboratory findings are presented in Table 5. The mean WBC was 9.95 before cerclage and elevated to

10.91 one day post cerclage and 11.2 on the second-day post cerclage. Regarding the CRP, the mean was 4.43 before the cerclage and increased to 10.2 on the first-day post cerclage. Then 11.1 the second day post cerclage.

Table 5. The laboratory findings among participants

Variables	Laboratory investigation		
	Before cerclage	**1 day post cerclage**	**2-day post cerclage**
WBC (Mean ± SD)	9.94 ±1.73	10.91± 1.81	11.2 ±2.14
CRP (Mean ± SD)	4.43 ± 2.1	10.2 ±2.1	11.1± 2.2

The association between the WBC level and prematurity is presented in Table 6. There is a significant difference in the WBC count on the second day post cerclage among women who had early premature delivery and women who delivered after 34 weeks of gestation Since the P value <0.05

However, there is no significant difference in the WBC level between the two groups before cerclage on the first-day post cerclage since the P value >0.05.

Table 6. The association between the WBC level and the date of delivery

Variables		**Gestational age at delivery**		**p-value**
		GA <34 weeks	GA≥ 34 weeks	
WBC	Before cerclage	9.48 ±1.55	10.55 ±1.76	**0.325**
	1 day post cerclage	11.64 ±1.9	10.75 ±1.75	**0.162**
	2-day post	14.44 ±1.45	10.47 ±1.49	**0.05**

The association between the CRP level and prematurity is presented in Table 7. There is a significant difference in the CRP at the first and second-day post cerclage among women who had early premature delivery and women who delivered after 34 weeks of gestation Since the P value <0.05

But there is no significant difference in the CRP level between the two groups before cerclage since P value >0.05

Table 7. The association between the CRP level and the date of delivery

Variables		**Gestational age at delivery**		**p-value**
		GA <34 weeks	**GA≥ 34 weeks**	
CRP	Before cerclage	4.06 ±0.6	4.52 ± 0.58	0.321
	1 day post cerclage	27.64 ±12.34	4.65 ±1.57	0.001
	2-day post	54.9 ±14.49	4.82 ±1.26	0.001

The mode of delivery among participants presented in Table 8, around two-thirds of women were delivered through normal vaginal delivery.

Table 8. The mode of delivery among participants

		Number	Percentage
Mode of delivery	NVD	40	**74.1**
	CS	14	**25.9**
	Total	54	**100.0**

Figure 1 shows the fate of the babies who delivered to the participant women. 8 babies died.

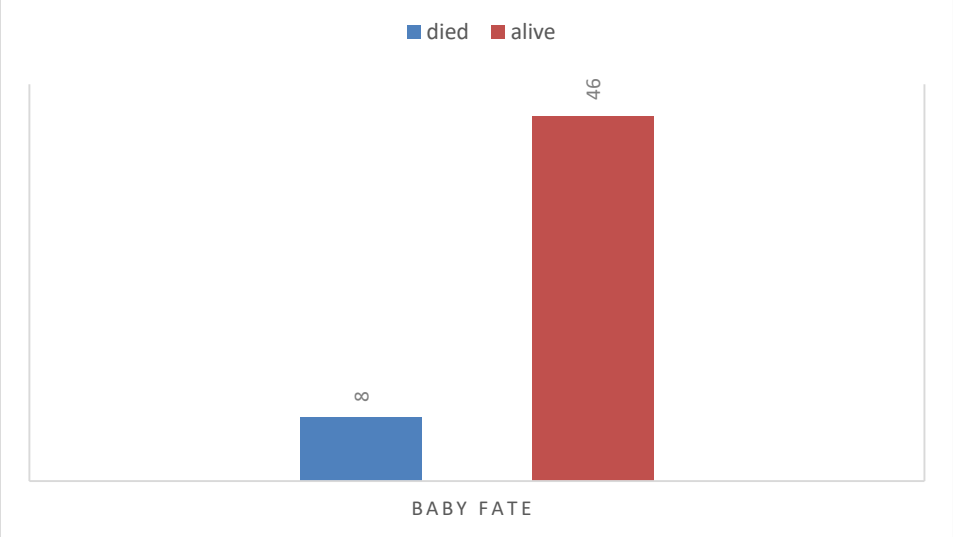

Figure 1. The baby's fate

4. DISCUSSION

Preterm birth is a major public health concern. Understanding the role of inflammatory markers in preterm labor is essential for optimizing management strategies and improving neonatal outcomes [9]. This study investigated the changes in C-reactive protein (CRP) and white blood cell (WBC) counts before and after indicated cervical cerclage and their potential predictive value for Early Preterm Birth. Our findings provide insights into the sociodemographic and clinical variables of the study population, the impact of cervical cerclage on pregnancy outcomes, and the association of CRP and WBC levels with gestational age at delivery.

Regarding the sociodemographic Characteristics (Table 1), the majority of participants were housewives (66.7%) and resided in urban areas (55.6%). Over half of the participants (51.9%) were illiterate, and only 11.1% had a college-level education or higher. These sociodemographic characteristics highlight a population with limited educational and occupational opportunities, which could influence access to antenatal care (ANC) and awareness of health practices [10]. These findings align with a previous study conducted in similar socioeconomic settings by Wekere et al. (2020), emphasizing the importance of tailoring interventions to address disparities in maternal health access [11].

In term of clinical variables and pregnancy characteristics (Tables 2 and 3), most participants (62.9%) had adequate ANC, and 70.4% were multiparous (1–4 children), suggesting that parity did not deter access to care. The cervical length increased significantly from 20.6 mm pre-cerclage to 23.8 mm post-cerclage, demonstrating the efficacy of the procedure in improving cervical competence which is in line

with the findings of Hulshoff et al. (2023) [12]. Despite this intervention, 18.5% of women experienced early preterm birth (<34 weeks) which is in agreement to what reported by Alfirevic et al. (2017) [13]. The mean gestational age at cerclage (20.6 weeks) and at delivery (35.3 weeks) are consistent with a study by Huang et al. (2021) [14], reporting cerclage timing and outcomes. However, the relatively high rate of preterm delivery warrants further investigation into additional contributing factors, including inflammatory and sociodemographic variables.

In regard to the anthropometric characteristics (Table 4), the mean BMI of 31.0 indicates that the majority of participants were overweight or obese (72.2%). Obesity is a known risk factor for adverse pregnancy outcomes, including preterm labor as reported by Persson et al. (2012) [15]. These findings underscore the need for weight management programs and nutritional counselling in pre-conception and antenatal care to mitigate risks.

About the laboratory findings (Tables 5, 6, and 7), the study found significant elevations in both WBC and CRP levels post-cerclage, particularly in women who delivered preterm. WBC counts increased significantly on the second day post-cerclage among women who experienced preterm birth (<34 weeks), suggesting an association between heightened inflammatory responses and early delivery.

Similarly, CRP levels showed a marked increase on the first- and second-days post-cerclage in the preterm group, with levels significantly higher than those who delivered after 34 weeks. These findings are consistent with the literature indicating that systemic inflammation, reflected by elevated CRP and WBC levels, plays a role in preterm labor (Fan et al., 2024 and Lee et al., 2023) [16, 17].

A study by Gomez-Lopez et al. (2022) [18] . highlighted the role of inflammatory markers in predicting adverse pregnancy outcomes, particularly in the context of cervical insufficiency and preterm birth. The elevated CRP and WBC levels could be indicative of subclinical infection or inflammatory activation triggered by the cerclage procedure. However, the absence of significant differences in pre-cerclage levels suggests that the inflammatory response post-cerclage is critical in predicting outcomes.

The association between elevated CRP and WBC levels with preterm birth aligns with findings from other studies, which emphasize the role of systemic inflammation as both a marker and a potential mediator of preterm labor. For instance, a study by Najat et al. (2014) [19]demonstrated that elevated CRP levels could predict preterm delivery in women undergoing cerclage. However, discrepancies in gestational age thresholds, study populations, and methodological differences may account for variations in predictive accuracy.

Regarding the mode of delivery and neonatal outcomes (Table 8 and Figure 1), the majority of participants delivered vaginally (74.1%), with caesarean sections performed in 25.9%. Despite the high rate of preterm births, this distribution aligns with the literature on cervical cerclage outcomes, where vaginal delivery is common unless complications arise. Notably, 8 neonatal deaths were reported, reflecting the severe consequences of preterm birth. These findings emphasize the critical need for early identification of at-risk pregnancies and targeted interventions to improve neonatal survival .

The findings of this study highlight the importance of monitoring inflammatory markers in women undergoing cervical cerclage. Elevated CRP and WBC levels post-cerclage may serve as early warning signs of impending preterm labor, prompting timely intervention. Despite the procedure's benefits in prolonging pregnancy, systemic inflammation post-cerclage appears to play a significant role in determining outcomes. Addressing underlying inflammatory and sociodemographic factors is essential for optimizing care and reducing the burden of preterm birth.

5. Limitations

This study has several limitations that should be considered when interpreting the findings. First, the sample size was relatively small (54 participants), which may limit the generalizability of the results to larger and more diverse populations. Second, the study was conducted in a specific socioeconomic and geographic setting, which may not reflect broader contexts. Third, potential confounding factors, such as maternal comorbidities, detailed infection status, or other inflammatory markers, were not extensively assessed, which could influence the inflammatory response and pregnancy outcomes. Additionally, while the study identified associations between inflammatory markers and preterm birth, the observational design does not establish causality.

6. Conclusions

Elevated CRP and WBC levels post-cervical cerclage are significantly associated with an increased risk of Early Preterm Birth. Cervical cerclage effectively increased cervical length, but a substantial proportion of women still experienced early preterm delivery, indicating the need for adjunctive strategies. Sociodemographic factors, including education and BMI, as well as inflammatory markers, play a crucial role in pregnancy outcomes in this population. The findings highlight the potential of CRP and WBC as predictive markers for preterm birth in women undergoing cerclage.

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Ethical Consideration: The ethical committee approved the study at. Obstetrics and Gynecology Department, College of Medicine.

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