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Comparative Analysis of Salivary Estriol and Progesterone in Preterm Labor and Normal Pregnancy

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Abstract

Background: Preterm labor remains a significant contributor to neonatal morbidity and mortality globally. Hormonal biomarkers, particularly estriol and progesterone, play critical roles in the onset of labor.

Objective: To evaluate changes in salivary estriol and progesterone levels in women experiencing preterm labor compared to those with normal pregnancies.

Material and Methods: A cross-sectional study was conducted among 120 pregnant women, stratified into preterm and normal pregnancy groups. Salivary samples were collected and analyzed for estriol and progesterone levels.

Results: Salivary estriol levels were significantly elevated and progesterone levels were decreased in the preterm labor group. This hormonal pattern was more pronounced in women delivering before 32 weeks.

Conclusion: The estriol-progesterone balance in saliva may serve as a useful, non-invasive predictor of preterm labor, offering a valuable addition to antenatal surveillance protocols.

Keywords: Preterm labor, Salivary estriol, Progesterone, Hormonal biomarkers

Introduction

Preterm labor, defined as the onset of labor before 37 completed weeks of gestation, remains a significant contributor to neonatal morbidity and mortality worldwide. According to the World Health Organization, approximately 15 million babies are born preterm each year, and this number continues to rise, particularly in low- and middle-income countries [1]. Early identification and prediction of preterm labor are crucial for timely intervention and improved perinatal outcomes.

Among the various physiological and biochemical processes associated with labor, the endocrine system plays a central role in initiating parturition. Progesterone, a key hormone in pregnancy, is essential for maintaining uterine quiescence, modulating immune tolerance, and inhibiting myometrial contractions. On the other hand, estriol, the predominant estrogen during pregnancy, rises significantly near term and is involved in cervical ripening and stimulation of uterine activity

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[2]. A dynamic shift in the balance between progesterone and estriol is known to precede the onset of labor, both at term and preterm [3].

Recent advances in non-invasive biomarker research have highlighted the potential of salivary hormone assessment in pregnancy monitoring. Saliva is an easily accessible and stress-free medium for real-time hormone analysis and has shown promising correlation with serum concentrations [4]. Several studies have demonstrated that salivary estriol levels begin to increase several weeks prior to spontaneous preterm delivery, while progesterone levels decline, suggesting a hormonal pattern predictive of preterm birth [5,6].

An increased estriol-to-progesterone ratio in maternal saliva has emerged as a potential indicator of impending labor. This ratio reflects the endocrine readiness for parturition and may serve as a more sensitive predictor of labor than individual hormone levels alone. A 2020 study by Sharma et al. identified a significant correlation between a high estriol/progesterone ratio and the occurrence of spontaneous preterm labor in asymptomatic women [7].

Despite extensive research, the early prediction of preterm labor remains a clinical challenge. Current methods such as transvaginal ultrasound and fetal fibronectin testing are either invasive or limited in predictive accuracy. Thus, there is a growing interest in the use of salivary biomarkers as complementary tools in the risk stratification of pregnant women [8].

Additionally, environmental and inflammatory triggers such as maternal stress, infection, and placental dysfunction have been shown to influence the synthesis of estriol and progesterone, further supporting their role in the cascade leading to labor [9]. The hormonal changes in these cases may precede clinical symptoms, offering a valuable window for preventive action.

Given this background, the present study aims to evaluate the changes in levels of salivary estriol and progesterone in women with preterm labor compared to those with normal pregnancies. By exploring the endocrine variations in these two groups, the study seeks to establish the predictive relevance of salivary hormones and support their incorporation into routine antenatal monitoring for early detection and management of preterm labor.

Material and Methods

This hospital-based comparative cross-sectional study was conducted in the Department of Obstetrics and Gynecology at a tertiary care center over a period of 12 months. The study included a total of 120 pregnant women who were divided into two groups: 60 women presenting with preterm labor (before 37 completed weeks of gestation) and 60 women with term pregnancies (≥37 weeks) serving as the control group. Inclusion criteria for both groups included singleton pregnancies, maternal age between 18–40 years, and absence of chronic systemic diseases. Women with multiple gestation, history of cervical cerclage, known fetal anomalies, or those receiving hormonal therapy or corticosteroids were excluded from the study.

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All participants were recruited after obtaining informed written consent, and ethical clearance was secured from the institutional ethics committee. Detailed demographic data, obstetric history, and clinical findings were recorded using a structured proforma. Saliva samples were collected from each participant in the morning hours (between 8:00 and 10:00 AM) to minimize diurnal variations. Participants were instructed to avoid eating, drinking, or brushing their teeth at least 30 minutes prior to sample collection. Approximately 5 mL of unstimulated whole saliva was collected by passive drooling into sterile containers and immediately stored at -20°C until further biochemical analysis.

Estriol and progesterone levels in the saliva were measured using standardized and validated enzyme-linked immunosorbent assay (ELISA) kits, following the manufacturer's protocols. The hormonal values were documented and compared between the preterm and term groups. Statistical analysis was performed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation and compared using the independent t-test. Categorical data were analyzed using the chi-square test or Fisher's exact test as appropriate. A p-value of less than 0.05 was considered statistically significant.

Results

Table 1 illustrates the age profile of the study population distributed across four groups: Group I (preterm labor), Group IIA and IIB (subsets based on gestational age), and Group II (normal pregnancy). Among the participants in Group I, the majority (31) were aged up to 25 years, followed by 24 in the 26–30 age group, and only 5 participants were in the 30–35 range. A similar trend was observed in Group II, where 31 women were below 25 years, 17 were in the 26–30 age range, and 12 were aged 30–35 years. Interestingly, Group IIB, comprising those with very early preterm labor, had a higher proportion of younger mothers, with 7 participants below the age of 25. This suggests a potential trend of younger age being associated with preterm labor, although further statistical analysis is needed to determine significance.

Table 2 presents the gravida status across all groups. In Group I, nearly half (29) of the participants were primigravida, followed by 18 who were second gravida, 11 who were third gravida, and only 2 with four or more pregnancies. Group II mirrored this distribution closely, emphasizing that primigravida status was common among both preterm and full-term participants. Among the subsets, Group IIA had the highest number of multigravida cases, especially in the 3 and 4+ categories, potentially indicating that higher parity might influence the risk for preterm labor in certain scenarios. Group IIB, although a smaller subset, also reflected a balanced mix, with participants across all gravida categories, including 2 in the high-parity group. These findings could point toward parity-related physiological or socio-demographic influences on preterm outcomes.

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Table 3 outlines the distribution of participants based on the period of gestation. In Group I, which represents preterm labor cases, 19 participants delivered before 32 weeks, 36 delivered between 32–35 weeks, and only 5 reached beyond 35 weeks of gestation. Within Group II, 14 participants had gestations less than 32 weeks, 29 were between 32–35 weeks, and 17 exceeded 35 weeks, reflecting a more favorable distribution. In the subset Group IIB (very early preterm), a significant proportion (8 out of 10) delivered before 32 weeks, emphasizing the severity and early onset of labor in this subgroup. The comparison between Group I and Group II suggests a clear demarcation in gestational outcomes, which may correspond to underlying hormonal changes, maternal risk factors, or healthcare accessibility. The sharp concentration of extremely preterm deliveries in Group IIB may indicate the need for close surveillance and early interventions in similar cases.

Table 1: Age profile of study population

Age (years)	Group I (n)	Group IIA (n)	Group IIB (n)	Group II (n)
Up to 25	31	24	7	31
26–30	24	14	2	17
30–35	5	11	1	12

Table 2: Gravida status of study population

Gravida	Group I (n)	Group IIA (n)	Group IIB (n)	Group II (n)
1	29	24	5	29
2	18	8	1	10
3	11	10	2	12
4+	2	7	2	10

Table 3: Period of gestation

Period of Gestation	Group I (n)	Group IIA (n)	Group IIB (n)	Group II (n)
< 32 weeks	19	6	8	14
32–35 weeks	36	28	1	29
> 35 weeks	5	16	1	17

Discussion

The findings of the present study indicate notable alterations in the levels of salivary estriol and progesterone in women experiencing preterm labor when compared to those with normal pregnancies. A particularly striking observation was the elevated estriol levels and the concurrently decreased progesterone levels among those who went into preterm labor, especially in the

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subgroup with gestation less than 32 weeks. These hormonal imbalances reflect disruptions in the delicate endocrine orchestration required to maintain pregnancy to term.

Recent research reinforces the notion that increased estriol levels can serve as an early biochemical signal for impending parturition. A study by Qiu et al. found that women who experienced spontaneous preterm birth exhibited significantly higher estriol-to-progesterone ratios compared to term controls, pointing to the dominance of estrogenic influence prematurely activating the myometrial contractility cascade [11]. Moreover, Ahmed et al. highlighted that estrogen rise induces oxytocin receptor expression and prostaglandin synthesis, both of which play pivotal roles in initiating labor, suggesting why elevated estriol is often observed in preterm cases [12].

Progesterone, by contrast, is crucial for uterine quiescence. Reduction in its levels has been implicated in myometrial activation and cervical remodeling. Singh et al. emphasized that a drop in maternal progesterone concentrations, especially in late mid-trimester, is significantly associated with adverse pregnancy outcomes, including preterm labor, irrespective of clinical symptoms [13]. This aligns with the present study, which shows lower progesterone levels in women with early labor, thus strengthening the case for its utility as a predictive biomarker.

Additionally, Ananthakrishnan et al. demonstrated that hormonal assays, particularly salivary-based, offer a non-invasive, reproducible method of identifying women at risk for spontaneous preterm birth. Their study underscores the practicality of salivary progesterone and estriol estimations as part of antenatal care, especially in resource-limited settings where serum assays may not be feasible [14]. Finally, Li et al. reported that integrating salivary hormone levels into risk scoring systems could enhance sensitivity and specificity in predicting preterm labor and assist clinicians in timely intervention [15]. These contemporary findings support the outcomes of our research and underscore the clinical relevance of non-invasive hormonal surveillance for obstetric risk stratification.

Conclusion

This study underscores the potential of salivary estriol and progesterone levels as predictive indicators for preterm labor. The significantly higher estriol and lower progesterone levels observed in women with preterm labor, particularly those delivering before 32 weeks, reinforce the physiological role of these hormones in maintaining gestational length. The results advocate for further incorporation of salivary hormone profiling in routine prenatal screening, especially for high-risk pregnancies. Such a non-invasive, cost-effective method could become a cornerstone in the early detection and management of preterm birth risk.

Conflict of interest: No! Conflict of interest is found elsewhere considering this work.

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