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COMPARISON OF ROLE OF HUMAN CHORIONIC GONADOTROPIN (HCG) AND PROGESTERONE IN PREVENTING PRETERM LABOR

Original Research

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ABSTRACT

Background: Preterm labor, defined as delivery before 37 weeks of gestation, remains a significant contributor to neonatal morbidity and mortality worldwide, especially in developing countries. It accounts for over two-thirds of all perinatal deaths and poses ongoing clinical and public health challenges. Pharmacological agents like progesterone and human chorionic gonadotropin (hCG) have been explored for their role in delaying preterm birth, yet area-specific data on their comparative efficacy remains limited.

Objective: To evaluate and compare the efficacy of hCG and vaginal progesterone in the prevention of preterm labor in pregnant women at risk.

Methods: This randomized controlled trial was conducted at the Department of Obstetrics and Gynecology, Saidu Group of Teaching Hospital, Saidu Sharif, Swat, from July 1st to December 31st, 2024. A total of 174 pregnant women aged 20–40 years, with gestational age between 16 and 36 weeks and parity up to four, were enrolled using non-probability consecutive sampling and randomized into two equal groups. Group A received 200 mg vaginal progesterone daily, and Group B received 5000 IU intramuscular hCG weekly with an adjunctive 100,000 IU infusion. Participants were followed every two weeks until 37 weeks. Data analysis was performed using SPSS version 24.

Results: The mean age was 29.98 ± 4.46 years in the progesterone group and 30.67 ± 5.55 years in the hCG group. Preterm labor was prevented in 32 out of 87 patients (35.6%) in the progesterone group, compared to 58 out of 87 patients (64.4%) in the hCG group ($p = 0.000$), indicating significantly higher efficacy of hCG.

Conclusion: hCG was more effective than vaginal progesterone in preventing preterm labor and extending gestation to term in the studied cohort.

Keywords: Gestational Age, Human Chorionic Gonadotropin, Parity, Preterm Labor, Progesterone, Tocolysis, Uterine Contraction.

INTRODUCTION

Preterm labor, defined as the onset of labor between 20 and 37 weeks of gestation, remains a significant global health concern. Despite accounting for only about 10% of all births, it contributes to nearly 70% of neonatal deaths, marking it as a critical indicator in global health assessments (1). The burden is particularly severe in underdeveloped regions, where access to advanced neonatal care is limited, further compounding the medical, financial, and societal implications of premature birth (2). Although technological and therapeutic advancements have improved maternal and neonatal outcomes, the incidence of preterm birth and its associated morbidity and mortality has remained largely unchanged in recent decades (3). This persistent challenge underscores the need for effective, affordable, and context-appropriate interventions that can be integrated into resource-constrained healthcare systems. Pharmacologic strategies have gained prominence in recent years, with progesterone and human chorionic gonadotropin (hCG) emerging as potential agents in the prevention of preterm labor (4). hCG, a glycoprotein hormone secreted primarily by the placenta, plays a crucial role in maintaining early pregnancy. During the later stages of gestation, it contributes to uterine quiescence by inhibiting myometrial contractions in a dose-dependent manner. Notably, a reduction in hCG receptors within the uterine myometrium has been observed with the onset of both term and preterm labor, suggesting a physiological role in the regulation of uterine activity (5,6). Clinical investigations have demonstrated promising results; a study reported that preterm labor was successfully prevented in over half of the cases following hCG administration (7).

Similarly, progesterone, known for its role in maintaining uterine stability and suppressing inflammatory responses, has been studied extensively. Danielle and colleagues found that vaginal progesterone prevented preterm labor in approximately one-third of patients at risk, supporting its potential as a prophylactic treatment (8-10). While these findings are encouraging, variability in patient populations, administration routes, and clinical settings has led to inconsistent outcomes, highlighting the need for further evaluation. There remains a critical gap in region-specific data regarding the efficacy of these agents in populations with high preterm birth rates and limited perinatal care infrastructure. Addressing this void is essential not only to optimize treatment strategies but also to reduce the emotional and physical toll associated with neonatal loss due to prematurity. Thus, this study aims to evaluate and compare the effectiveness of hCG and progesterone in preventing preterm labor, with the goal of informing clinical practice and offering evidence-based hope to families at risk of preterm birth.

METHODS

This randomized controlled trial was conducted at the Department of Obstetrics and Gynecology, Saidu Group of Teaching Hospital (SGTH), Saidu Sharif, Swat, from July 1st to December 31st, 2024. The study aimed to evaluate and compare the efficacy of vaginal progesterone and human chorionic gonadotropin (hCG) in the prevention of preterm labor. A total of 174 pregnant women were enrolled using non-probability consecutive sampling, with 87 participants allocated to each treatment arm. Inclusion criteria comprised pregnant women aged 20 to 40 years, with a gestational age between 16 and 36 weeks and parity up to four, who presented for antenatal care during the study period. Patients were excluded if they had abnormal vaginal bleeding, ectopic pregnancy, ruptured membranes, multiple gestation, or if they were already receiving progesterone or hCG therapy (11). The diagnosis of preterm labor was based on the presence of regular uterine contractions accompanied by cervical changes and descent of the presenting part before 37 completed weeks of gestation. The primary outcome measure was the prevention of preterm labor, defined as the successful prolongation of pregnancy to at least 37 weeks of gestation. Efficacy was considered achieved if no labor occurred before 37 weeks, according to the operational definition.

After obtaining approval from the hospital's Institutional Review Board and Ethics Committee, eligible participants were counseled, and informed written consent was obtained. Patient confidentiality and the voluntary nature of participation were emphasized throughout the study. Baseline demographic and clinical characteristics were recorded, including age, parity, gestational age, BMI (kg/m²), domicile (urban or rural), educational level, occupation, monthly income, and socioeconomic status. Block randomization was employed to allocate participants evenly into two groups. Group A received 200 mg of vaginal progesterone administered at bedtime daily, while Group B received weekly intramuscular injections of 5000 IU of hCG along with a 100,000 IU infusion in 500 ml of 5% dextrose,

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administered at a rate of 20 drops per minute. Follow-up assessments were conducted biweekly until 37 weeks of gestation, and outcomes were recorded to determine whether preterm labor was successfully prevented. Data were analyzed using IBM SPSS version 24. Continuous variables such as age, BMI, and gestational age were summarized using means and standard deviations, while categorical variables like parity, efficacy, domicile, occupation, education, and socioeconomic status were presented as frequencies and percentages. Comparative analysis between the two treatment groups was performed using the chi-square test. Post-stratification chi-square tests were also applied to assess the influence of effect modifiers such as age, BMI, parity, and gestational age on treatment efficacy. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The study enrolled 174 pregnant women, with 87 participants in each treatment group. The mean age in the progesterone group was 29.98 ± 4.46 years, while it was slightly higher in the hCG group at 30.67 ± 5.55 years. The average BMI was significantly different between the groups, recorded as 22.29 ± 1.94 kg/m² in the progesterone group and 24.94 ± 2.63 kg/m² in the hCG group. Similarly, the mean gestational age at enrollment was 28.87 ± 3.06 weeks for those receiving progesterone and 27.39 ± 4.15 weeks for those administered hCG. Among participants, 50 women (57.5%) in the progesterone group and 46 women (52.9%) in the hCG group were older than 30 years (p = 0.542), showing no significant age-based difference. Gestational age beyond 30 weeks was seen in 63 women (72.4%) in the progesterone group compared to 51 women (58.6%) in the hCG group, which approached statistical significance (p = 0.056). A notable difference was observed in BMI distribution: only 8 participants (9.2%) in the progesterone group had a BMI greater than 25.0 kg/m² compared to 42 participants (48.3%) in the hCG group, which was statistically significant (p = 0.000). Parity was another distinguishing factor; 56 participants (64.4%) in the progesterone group had a parity of 3 or less, compared to only 40 (46.0%) in the hCG group (p = 0.015). Regarding education status, 53 women (60.9%) in the progesterone group and 67 women (77.0%) in the hCG group were educated, with a statistically significant difference (p = 0.022). Employment status was not significantly different between groups (p = 0.562). The primary outcome—prevention of preterm labor—was observed in 32 participants (35.6%) treated with progesterone and 58 participants (64.4%) treated with hCG, which was statistically significant (p = 0.000), suggesting superior efficacy of hCG in prolonging gestation until 37 weeks.

Table 1: Descriptive statistics of study participants (n = 174)

Group		Mean	Std. Deviation
Progesterone (n = 87)	Age (years)	29.98	4.464
	PoG (weeks)	28.87	3.057
	BMI (kg/m^2)	22.293	1.9446
hCG (n = 87)	Age (years)	30.67	5.548
	PoG (weeks)	27.39	4.152
	BMI (kg/m^2)	24.943	2.6358

Table 2: Baseline clinical and demographic characteristics of study participants (n = 174)

Parameters and subgroups		**Group**		**Total**	**P value**
		Progesterone (n = 87)	**hCG (n = 87)**		
Age (years)	30 or below	37	41	78	0.542
		42.5%	47.1%	44.8%	
	More than 30	50	46	96	
		57.5%	52.9%	55.2%	
Gestational age (weeks)	30 or below	24	36	60	0.056
		27.6%	41.4%	34.5%	
	More than 30	63	51	114	
		72.4%	58.6%	65.5%	
Parity	3 or below	56	40	96	0.015
		64.4%	46.0%	55.2%	

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Parameters and subgroups		Group		Total	P value
		Progesterone (n = 87)	hCG (n = 87)		
	More than 3	31	47	78	
		35.6%	54.0%	44.8%	
BMI (kg/m^2)	25.0 or below	79	45	124	0.000
		90.8%	51.7%	71.3%	
	More than 25.0	8	42	50	
		9.2%	48.3%	28.7%	
Education	Yes	53	67	120	0.022
		60.9%	77.0%	69.0%	
	No	34	20	54	
		39.1%	23.0%	31.0%	
Profession	Employed	15	18	33	0.562
		17.2%	20.7%	19.0%	
	Unemployed	72	69	141	
		82.8%	79.3%	81.0%	

Table 3: Efficacy of progesterone and hCG in prevention of preterm labor (n = 174)

		Group		Total	P value
		Progesterone	hCG		
Efficacy	No	55	29	84	0.000
		65.5%	34.5%	100.0%	
	Yes	32	58	90	
		35.6%	64.4%	100.0%	
Total		87	87	174	
		50.0%	50.0%	100.0%	

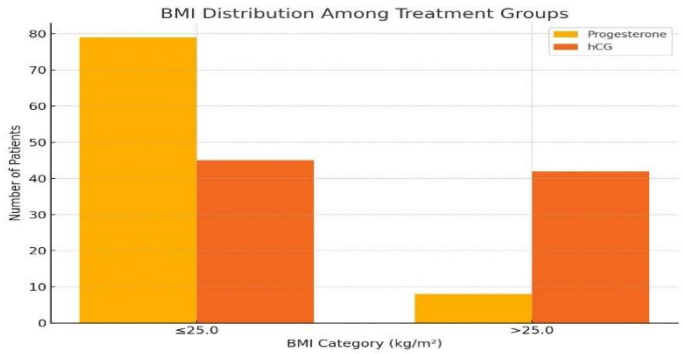

Figure 1 BMI Distribution Among Treatment Groups

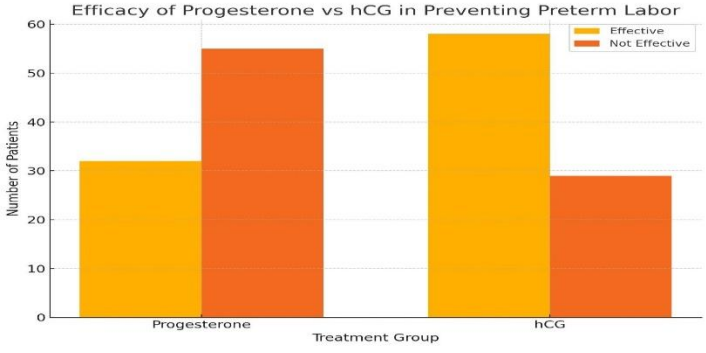

Figure 2 Efficacy of Progesterone vs hCG in Preventing Preterm Labor

DISCUSSION

Preterm delivery remains a leading contributor to infant mortality and long-term morbidity, particularly in developing countries where healthcare infrastructure is often inadequate. Despite significant advancements in obstetric care, preterm birth continues to account for over two-thirds of perinatal deaths globally (12). Its increasing incidence, particularly in low-resource settings where it ranges from 7.4% to 13.3% of births compared to 8.6% in high-income nations, underscores the urgent need for effective preventive strategies (13). The clinical consequences of preterm birth are profound, including respiratory distress syndrome, chronic lung disease, intraventricular hemorrhage, sepsis, and neurodevelopmental impairments, all of which burden neonatal health systems and families alike. Although a

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wide array of tocolytic agents have been employed in attempts to suppress preterm labor, few studies have directly compared agents within the same clinical context. In this trial, the efficacy of hCG was observed to be significantly superior to that of vaginal progesterone, with 64.4% of patients in the hCG group reaching full term compared to 35.6% in the progesterone group ($p = 0.000$). This finding is noteworthy, as earlier investigations have often reported relatively comparable live birth outcomes between the two interventions (14-16). The divergence in results could be attributed to differences in study populations, dosage protocols, or healthcare settings, which underscores the importance of context-specific evidence. Human chorionic gonadotropin plays a well-documented role in the maintenance of pregnancy, acting as a biochemical mediator of uterine quiescence during the third trimester. Several studies have demonstrated that hCG suppresses myometrial contractility in a concentration-dependent manner, thereby reducing the risk of premature labor (17,18). Beyond its mechanical effects, hCG modulates stromal differentiation and decidualization, which are critical to embryonic survival and uterine receptivity (19). Furthermore, hCG has been shown to enhance uterine perfusion by decreasing arterial impedance, reinforcing its utility in sustaining pregnancy during vulnerable gestational windows (20). The results of the current study provide additional clinical support for these mechanisms, positioning hCG as a physiologically favorable and clinically effective agent in the management of preterm labor.

The demographic profile of study participants aligns closely with previous literature, with the majority being above 30 years of age. This trend may reflect rising marital age in both national and international populations, contributing to an increasing number of pregnancies occurring at advanced maternal ages (21). The gestational age distribution, with most patients in the hCG group presenting after 30 weeks, is also consistent with earlier reports. However, while parity did not significantly differ between groups, BMI was markedly higher in the hCG group. This difference could have influenced drug pharmacodynamics and patient response and warrants further investigation. One of the strengths of this study is its randomized design and standardized follow-up, which enhanced the reliability of efficacy comparisons. Moreover, the study contributes novel region-specific data on the comparative performance of hCG and progesterone, which is particularly valuable in settings with high preterm birth rates and limited neonatal resources. However, the trial is not without limitations. The absence of blinding and reliance on non-probability sampling may introduce selection bias. Additionally, the potential confounding effect of BMI and other socioeconomic variables was not fully controlled. The study also did not stratify efficacy outcomes based on gestational age at enrollment or parity, which could have provided deeper insights into subgroup-specific responses. Future studies should consider multicenter designs with larger sample sizes, stratified randomization, and exploration of combination therapies or alternate dosing schedules (22). Investigation into the pharmacogenomic response to hCG and progesterone may also illuminate differential treatment effects across diverse populations. Despite these limitations, the current findings reaffirm the potential of hCG as a potent endogenous tocolytic and support its broader consideration in preterm labor management, particularly in resource-limited settings.

CONCLUSION

This study concludes that human chorionic gonadotropin (hCG) demonstrates superior efficacy compared to 17-alpha hydroxyprogesterone in preventing preterm labor among women at risk due to unexplained causes or suspected hormonal imbalance. While progesterone remains a cost-effective and convenient option, hCG offers more favorable pregnancy outcomes and may serve as a more reliable therapeutic choice in such cases. These findings support the broader consideration of hCG in clinical protocols aimed at reducing the burden of preterm birth, especially in populations where early identification and intervention can significantly improve neonatal health outcomes.

AUTHOR CONTRIBUTION

Author	Contribution
Rida Kumari	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Saima Parveen*	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Parveen Naveed	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Tabassum Ikram	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Komal Sabahat	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Zareena Shah	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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