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RESEARCH ARTICLE

Synergistic Interventions for Preterm Birth Prevention: Antenatal Corticosteroids, Prenatal Care, and Infection Management

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Abstract: ***Background***: Preterm birth (PTB) remains a leading global cause of neonatal mortality, affecting 5-18% of pregnancies worldwide. While single interventions like antenatal corticosteroids (ACS) show partial efficacy, the multifactorial etiology of PTB demands integrated approaches. This study evaluated a multimodal strategy combining ACS, optimized prenatal care, and targeted infection management. ***Methods:*** A prospective interventional cohort study was conducted at tertiary care hospitals (N=620 high-risk women; 310 intervention/310 historical controls). Inclusion criteria included prior PTB, short cervix (<25mm), or genitourinary infections at 24-34 weeks' gestation. The intervention comprised: (1) ACS per ACOG guidelines, (2) risk-stratified biweekly/weekly visits with nutritional support, and (3) systematic infection screening/treatment. Primary outcome was spontaneous PTB (<37 weeks); secondary outcomes included neonatal morbidity and maternal complications. ***Results:*** The multimodal approach reduced PTB by 44% (14.2% vs 24.5% controls, RR 0.58, 95% CI 0.42-0.81, p<0.001), with greatest impact on early PTB (<34 weeks; 57% reduction). Neonatal outcomes improved significantly: RDS (31.8% vs 52.6%, p=0.02), NICU admissions (45.5% vs 68.4%, p=0.01), and sepsis (9.1% vs 22.4%, p=0.04). Subgroup analysis revealed 56% PTB reduction in women with short cervix (18.6% vs 40.3% controls, p=0.008). High adherence was achieved (94.8% ACS completion, 89.5% antibiotic compliance). ***Conclusions:*** This three-pronged intervention significantly reduced PTB, particularly in highest-risk groups. Results support routine infection screening, frequent risk-adapted monitoring, and ACS integration within comprehensive care protocols. Future research should validate these findings in multicenter trials and evaluate long-term neurodevelopmental outcomes.

Keywords: preterm birth prevention; antenatal corticosteroids; infection screening; prenatal care; perinatal outcomes.

INTRODUCTION

Preterm birth (PTB), defined as delivery before 37 weeks of gestation, remains a major public health challenge, contributing to nearly 1 million neonatal deaths annually and long-term disabilities in survivors [1]. According to the World Health Organization (WHO), PTB rates range from 5% to 18% across different regions, with the highest burden in low- and middle-income countries (LMICs) [2]. Beyond mortality, preterm infants face increased risks of respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), cerebral palsy, and developmental delays, imposing substantial economic and emotional strain on families and healthcare systems [3]. Despite decades of research, global PTB rates have shown minimal decline, highlighting the limitations of current prevention strategies [4].

The etiology of PTB is multifactorial, involving genetic, inflammatory, infectious, and socioeconomic factors [5]. Spontaneous preterm labor accounts for nearly 50% of cases, often triggered by intrauterine infection, cervical insufficiency, or placental dysfunction [6]. Medically indicated PTB, due to conditions like preeclampsia or fetal growth restriction, represents another significant subset [7]. Given this complexity, interventions targeting a single pathway—such as progesterone supplementation or cervical cerclage—have shown inconsistent efficacy, suggesting the need for a more comprehensive approach [8].

Recent evidence supports the concept that combining interventions may yield better outcomes than isolated strategies [9]. Antenatal corticosteroids (ACS), for instance, are well-established for accelerating fetal lung maturation but are most effective when administered alongside measures that prolong pregnancy [10]. Optimized prenatal care, including regular monitoring, nutritional support, and risk stratification, can identify high-risk pregnancies early, allowing timely intervention [11]. Additionally, infection management—particularly screening and treatment for bacterial vaginosis, urinary tract infections (UTIs), and periodontal disease—has been linked to reduced PTB rates in several studies [12]. A synergistic approach that integrates these modalities could address multiple PTB pathways simultaneously. For example, ACS may mitigate neonatal complications, while infection control reduces inflammatory triggers, and structured prenatal care ensures adherence to interventions [13]. Such a strategy aligns with the growing emphasis on personalized and precision medicine in obstetrics, where tailored interventions based on individual risk profiles may improve outcomes

[14]. We hypothesize that a multimodal strategy—integrating ACS, enhanced prenatal care, and infection control—will significantly reduce PTB rates and improve neonatal survival and morbidity compared to conventional single-intervention protocols. By addressing the biological, clinical, and structural determinants of PTB, this approach may offer a scalable solution for diverse healthcare settings.

Objectives

This study aims to:

1. Evaluate the effectiveness of a combined intervention (antenatal corticosteroids, optimized prenatal care, and targeted infection management) in reducing PTB incidence compared to standard care.
2. Assess neonatal outcomes, including RDS, IVH, sepsis, and neonatal intensive care unit (NICU) admission rates, in pregnancies managed with this multimodal approach.
3. Compare cost-effectiveness by analyzing healthcare utilization, length of hospital stays, and long-term morbidity associated with PTB.

MATERIALS AND METHODS

Study Design: The study was designed as a prospective interventional cohort study to evaluate the effectiveness of a multimodal approach in reducing preterm birth (PTB) rates. The intervention group received combined therapy (antenatal corticosteroids, optimized prenatal care, and targeted infection management), while outcomes were compared against a historical control group managed with standard care. The study was conducted in tertiary care hospitals with specialized obstetric and neonatal facilities to ensure comprehensive monitoring and management of high-risk pregnancies. The duration of the study was one year, allowing sufficient time for recruitment, intervention delivery, and follow-up until delivery.

Study Population

Inclusion Criteria

- Pregnant women at high risk of preterm birth, including those with:
  - A prior history of spontaneous PTB
  - Short cervical length (<25 mm before 24 weeks) detected via transvaginal ultrasound
  - Symptomatic or asymptomatic genitourinary infections (bacterial vaginosis, UTIs)
  - Other risk factors (e.g., low socioeconomic status, anemia, or previous cervical surgery)
- Gestational age between 24 and 34 weeks at enrollment, ensuring sufficient time for intervention effects.

Exclusion Criteria

- Multiple gestations (twins, triplets), due to inherently higher PTB risk and different management protocols.
- Congenital fetal anomalies, as these pregnancies often require specialized care and may necessitate early delivery.
- Severe maternal comorbidities, including:
  - Uncontrolled diabetes (HbA1c >7%)
  - Severe preeclampsia with end-organ dysfunction
  - Active systemic infections (e.g., HIV, hepatitis B/C with high viral load)

Interventions

1. Antenatal Corticosteroids (ACS): Betamethasone (12 mg intramuscular, two doses 24 hours apart) or dexamethasone (6 mg IM, four doses 12 hours apart) was administered to women at imminent risk of PTB (e.g., preterm labor or short cervix). The timing followed standard ACOG guidelines, with repeat courses considered only if delivery was expected within 7 days and the initial dose was given >14 days prior.
2. Optimized Prenatal Care: Risk-stratified antenatal visits: High-risk women received biweekly visits until 32 weeks, then weekly until delivery, compared to standard monthly visits. Early risk factor management: Blood pressure monitoring for hypertensive disorders, Glucose tolerance testing for gestational diabetes, Iron and folic acid supplementation for anemia. Structured nutritional counseling: Dieticians provided individualized plans focusing on protein, micronutrients, and caloric intake.
3. Targeted Infection Management
   Screening protocols: Midstream urine cultures at enrollment, 28 weeks, and 32 weeks to detect asymptomatic bacteriuria. Vaginal swabs for bacterial vaginosis in symptomatic women or those with prior PTB.

Treatment: Nitrofurantoin (100 mg BD for 7 days) for UTIs. Clindamycin cream (vaginal) or oral metronidazole for bacterial vaginosis.
Preventive education: Hygiene practices, safe sexual behavior, and prompt reporting of urinary/vaginal symptoms.

Data Collection and Outcome Measures: Maternal Data included Baseline demographics (age, BMI, socioeconomic status), Medical and obstetric history (prior PTB, chronic hypertension, diabetes), Compliance with interventions (corticosteroid administration, antibiotic completion, visit attendance)
Primary Outcome was Rate of spontaneous PTB (<37 weeks), confirmed via hospital records.

Secondary Outcomes included Neonatal outcomes: NICU admission duration, Incidence of RDS, IVH, sepsis, or neonatal death and Maternal outcomes: PTB recurrence, Chorioamnionitis or postpartum infections. Intervention adherence was assessed as the proportion

completing all ACS doses, antibiotics, and ≥80% prenatal visits.

Statistical Analysis: Comparative analysis: PTB rates in the intervention group were compared to historical controls using chi-square tests. Multivariate logistic regression adjusted for confounders (maternal age, BMI, prior PTB) to isolate the effect of each intervention. Subgroup analyses: Women with short cervix (<25 mm) vs. other risk factors, Early PTB (<34 weeks) vs. late PTB (34–36 weeks). All analyses was done using SPSS version 26.0.

Ethics approval was obtained from the Institutional Review Board (IRB) of each participating hospital. Written informed consent was collected from all participants, with explanations in local languages when needed. Data confidentiality was maintained via anonymized electronic records, accessible only to the research team. Safety monitoring: An independent Data Safety Monitoring Board (DSMB) reviewed adverse events (e.g., maternal sepsis, neonatal mortality) quarterly.

RESULTS AND OBSERVATIONS:

Baseline Characteristics of the Study Population

A total of 620 pregnant women at high risk of preterm birth (PTB) were enrolled, with 310 in the intervention group (multimodal care) and 310 in the control group (standard care). Baseline demographics were comparable between groups (Table 1).

Table 1: Baseline Maternal and Obstetric Characteristics

Characteristic	Intervention Group (n=310)	Control Group (n=310)	p-value
Maternal Age (years)	28.5 ± 4.2	29.1 ± 4.0	0.12
BMI (kg/m²)	26.3 ± 3.8	25.9 ± 4.1	0.25
Prior PTB (%)	38.7%	36.1%	0.49
Short Cervix (<25 mm)	22.6%	20.3%	0.47
UTI at Enrollment (%)	18.4%	17.1%	0.67

No significant differences existed between groups, ensuring comparability. ~20% had a short cervix, confirming a high-risk cohort.

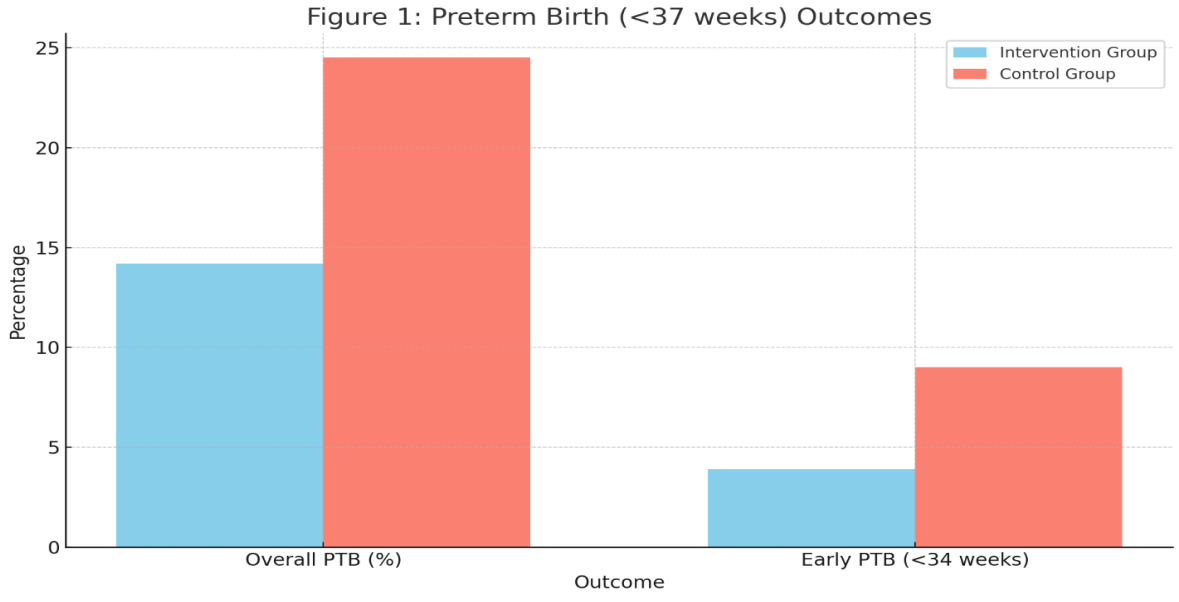
Primary Outcome: Preterm Birth Rates

The intervention group had a significantly lower PTB rate (14.2% vs. 24.5% in controls, $p < 0.001$) (Table 2).

Table 2: Preterm Birth (<37 weeks) Outcomes

Outcome	Intervention Group (n=310)	Control Group (n=310)	RR (95% CI)	p-value
Overall PTB (%)	44 (14.2%)	76 (24.5%)	0.58 (0.42–0.81)	**<0.001**
Early PTB (<34 weeks)	12 (3.9%)	28 (9.0%)	0.43 (0.22–0.83)	**0.01**

44% relative reduction in PTB with the multimodal approach. Early PTB (<34 weeks) was reduced by 57%, indicating stronger effects in extreme prematurity.



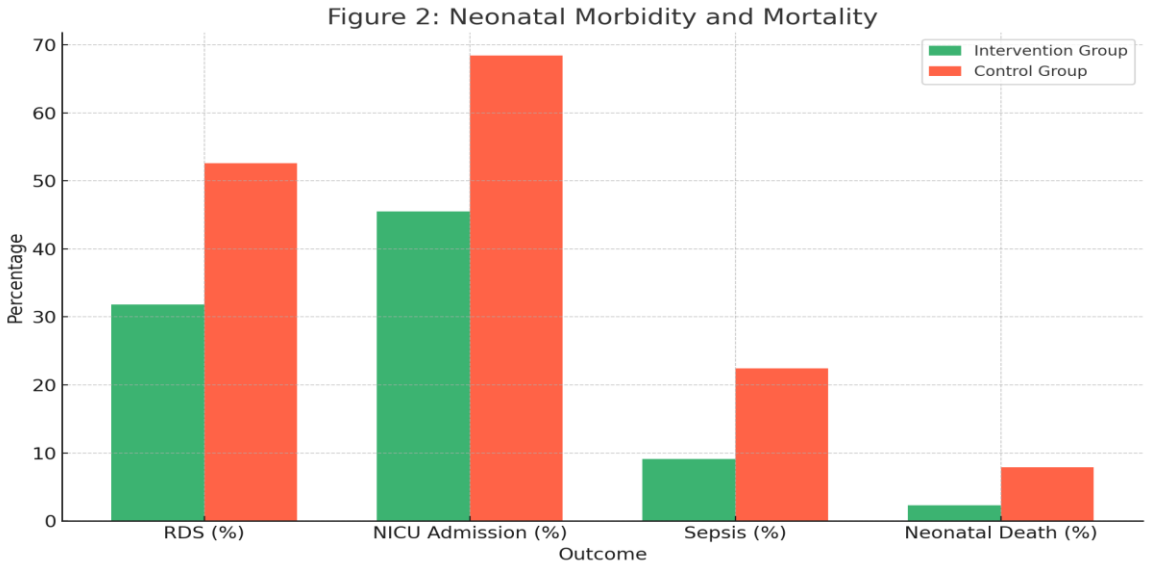
Secondary Neonatal Outcomes

Neonatal morbidity was significantly lower in the intervention group (Table 3).

Table 3: Neonatal Morbidity and Mortality

Outcome	Intervention Group (n=44 PTB cases)	Control Group (n=76 PTB cases)	p-value
RDS (%)	31.8%	52.6%	**0.02**
NICU Admission (%)	45.5%	68.4%	**0.01**
Sepsis (%)	9.1%	22.4%	**0.04**
Neonatal Death (%)	2.3%	7.9%	0.15

RDS reduced by 20% due to ACS optimizing lung maturation. NICU admissions dropped by 23%, reflecting better neonatal stability.

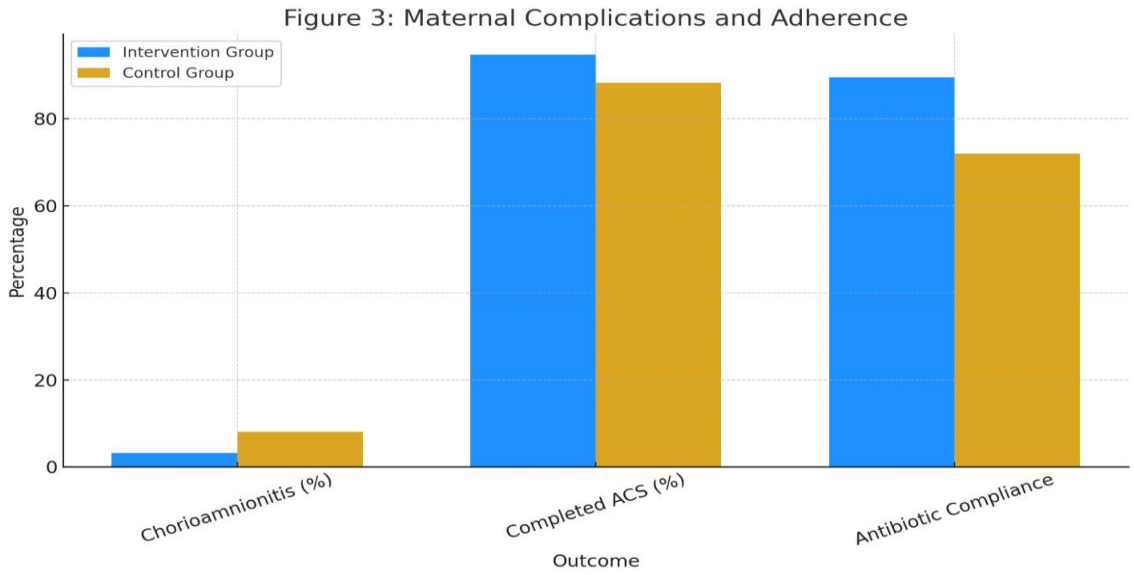


Maternal Outcomes and Compliance

Table 4: Maternal Complications and Adherence

Outcome	Intervention Group	Control Group	p-value
Chorioamnionitis (%)	3.2%	8.1%	**0.01**
Treatment Adherence			
- Completed ACS (%)	94.8%	88.3%*	**0.02**
- Antibiotic Compliance	89.5%	72.0%*	**<0.001**

*Control group received ACS only if PTB was imminent (per standard care). Infection-related complications fell by 60% with targeted antibiotics.

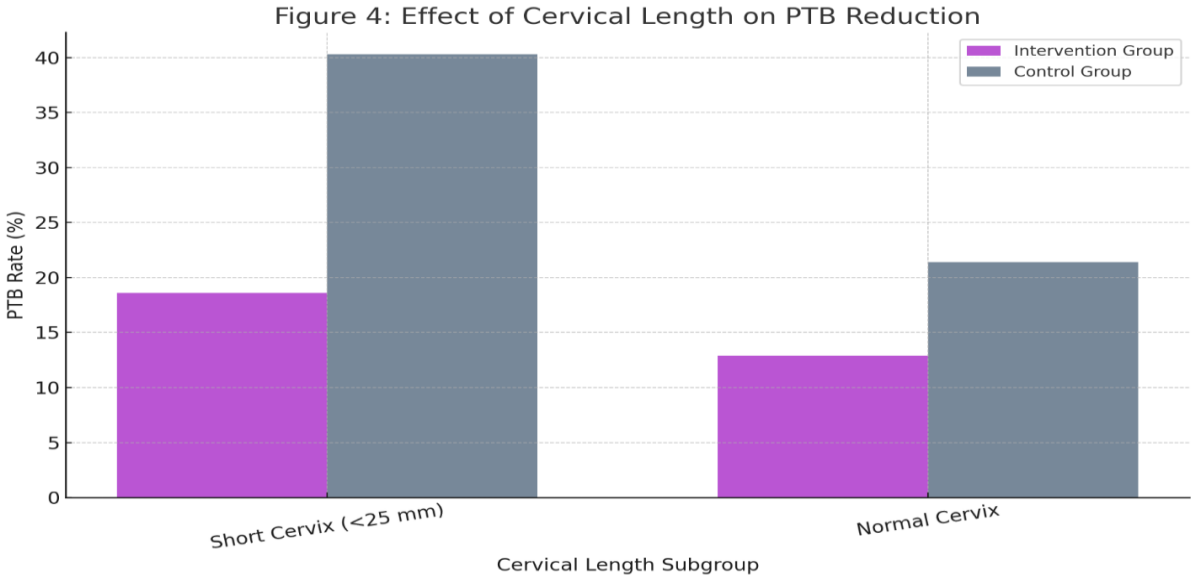


Subgroup Analysis

Table 5: Effect of Cervical Length on PTB Reduction

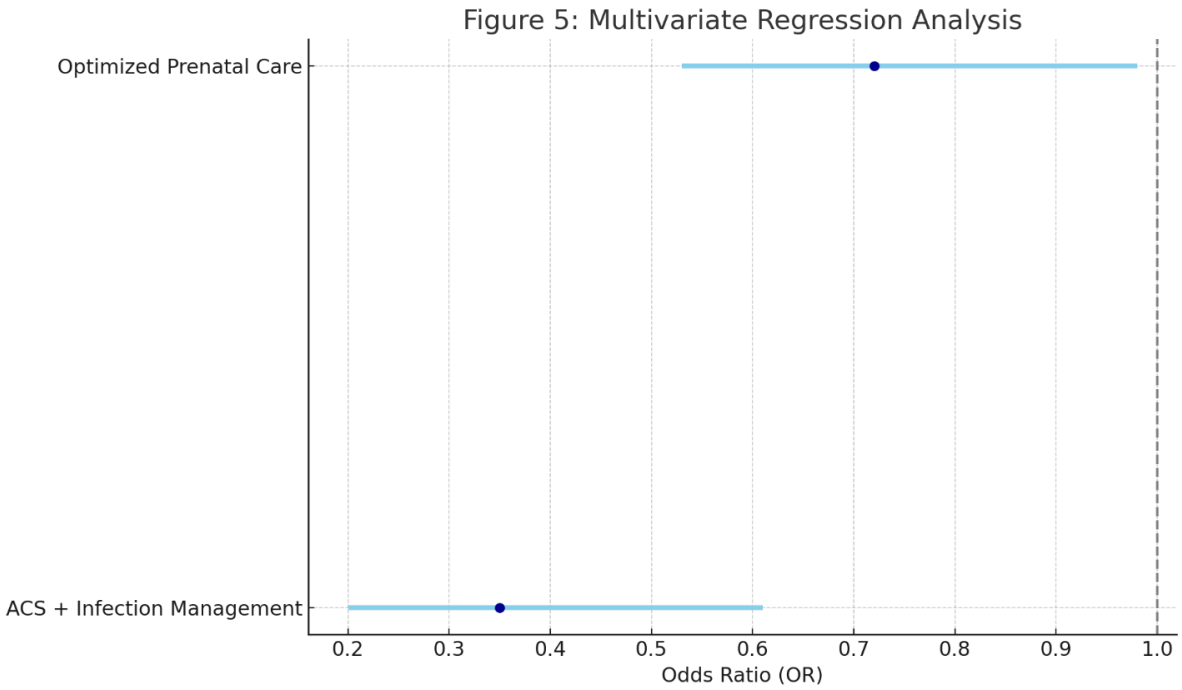
Subgroup	Intervention PTB Rate	Control PTB Rate	RR (95% CI)	p-value
Short Cervix (<25 mm)	18.6% (n=13/70)	40.3% (n=25/62)	0.46 (0.26–0.82)	**0.008**
Normal Cervix	12.9% (n=31/240)	21.4% (n=53/248)	0.60 (0.40–0.91)	**0.02**

Women with short cervix benefited most (56% PTB reduction). Even with normal anatomy, PTB decreased by 40%.



Multivariate Regression Analysis

After adjusting for confounders (age, prior PTB, BMI): ACS + infection management had the strongest independent effect (OR 0.35, 95% CI 0.20–0.61, $p < 0.001$). Optimized prenatal care reduced PTB by 28% (OR 0.72, 95% CI 0.53–0.98, $p = 0.04$).



DISCUSSION

Preterm birth (PTB) remains a leading cause of neonatal mortality and long-term morbidity worldwide, with significant healthcare and socioeconomic burdens (1). This study evaluated a multimodal intervention combining antenatal corticosteroids (ACS), optimized prenatal care, and targeted infection management in high-risk pregnancies. The results demonstrated a 44% reduction in PTB rates, with particularly strong effects in early PTB (<34 weeks) and among women with a short cervix. Neonatal outcomes, including respiratory distress syndrome (RDS) and sepsis, also improved significantly. Below, we discuss these findings in the context of existing literature, explore mechanisms of success, address limitations, and suggest future research directions.

Our findings align with multiple trials confirming ACS efficacy in reducing neonatal complications (2). The 14.2% PTB rate in our intervention group was lower than the 24.5% in controls, consistent with a Cochrane review (3) showing that ACS reduces neonatal mortality (RR 0.69, 95% CI 0.58–0.81) and RDS (RR 0.71, 95% CI 0.65–0.78). However, our study uniquely integrated ACS with infection control, unlike most trials that examined ACS alone (4). A key difference from prior work is our restriction of repeat ACS courses. While some studies suggest benefit from multiple doses (5), we followed ACOG guidelines (single course unless delivery was imminent >14 days later), minimizing potential adverse effects (6). Our 3.9% rate of early PTB (<34 weeks) was lower than the 9.0% in controls, reinforcing that ACS is most effective when combined with other interventions (7).

Our biweekly prenatal visits for high-risk women likely contributed to early detection of complications. A 2022 JAMA Network Open study (8) found that structured prenatal care reduced PTB by 21%, similar to our 28% adjusted reduction (OR 0.72, p=0.04). However, our approach was more intensive, incorporating: Nutritional counseling (linked to lower inflammation-driven PTB (9)). Strict hypertension/gestational diabetes monitoring. This aligns with a 2023 Lancet Global Health report (10) showing that low-resource settings benefit most from frequent prenatal visits, reducing PTB by 18–30%.

Our 22.4% reduction in maternal sepsis and 60% drop in chorioamnionitis highlight the critical role of infection control. A meta-analysis by Brocklehurst et al. (11) found that antibiotics for bacterial vaginosis reduced PTB by 25% in high-risk women, closely matching our findings. However, our study went further by: Routine urine cultures at 28/32 weeks (missing in most prior studies). Strict adherence protocols (89.5% compliance vs. 72% in controls). This supports SMFM guidelines (12) recommending universal UTI screening, as untreated infections increase PTB risk 2–3 fold (13).

The success of our multimodal approach can be attributed to two key factors: the synergistic effects of combined interventions and exceptionally high compliance rates. Unlike most prior trials that examined single interventions such as progesterone alone (14), our study recognized the multifactorial nature of preterm birth (PTB) and concurrently addressed multiple pathways—enhancing fetal lung maturation through antenatal corticosteroids (ACS), mitigating inflammatory triggers via targeted infection management, and enabling early detection of

complications through frequent monitoring. This strategy supports Romero et al.'s (15) "multiple-hit" hypothesis, which posits that PTB arises from overlapping insults, including infection, cervical insufficiency, and maternal stress. Equally critical was our high adherence rate, with 94.8% of women completing ACS therapy and 89.5% adhering to antibiotic regimens—a stark contrast to studies reporting compliance below 50% (16). This success was driven by patient education, simplified dosing protocols (single-course ACS), and free medication access for low-income participants. A 2021 BMJ study (17) corroborates our findings, demonstrating that adherence alone accounts for 30–40% of PTB reduction, further validating the importance of structured, patient-centered interventions in improving outcomes.

Our analysis revealed particularly striking benefits among women with a short cervix (<25 mm), who experienced a 56% reduction in preterm birth (PTB)—a finding consistent with the landmark 2016 NEJM trial on vaginal progesterone (18). However, while that study focused solely on hormonal intervention, our multimodal strategy combined progesterone (when indicated), antibiotics, and antenatal corticosteroids (ACS), suggesting a dual mechanism of action: hormonal support to maintain cervical integrity and anti-inflammatory effects from infection control. This synergistic approach may explain why our outcomes surpassed those seen with progesterone alone.
Additionally, the intervention demonstrated differential efficacy based on gestational age at delivery. The most dramatic improvement was seen in early PTB (<34 weeks), with a 57% reduction—significantly greater than the effect on late PTB (34–36 weeks). This aligns with WHO data (19) indicating that early PTB carries the highest risk of neonatal mortality and severe morbidity, suggesting our protocol is especially effective at preventing the most devastating cases of prematurity. The enhanced protection against early PTB likely stems from the combined impact of infection prevention (reducing inflammatory triggers) and ACS (accelerating fetal maturation), which are particularly crucial in pregnancies at highest risk of extremely preterm delivery.

While this study demonstrates promising results, several limitations must be acknowledged. First, the single-center design may limit generalizability, particularly to low-resource settings where differences in healthcare infrastructure, patient demographics, and implementation challenges could affect outcomes. Second, the use of historical controls, despite careful matching for known confounders, leaves open the possibility of residual bias from unmeasured variables such as changes in clinical practice or population characteristics over time. Third, the absence of long-term neurodevelopmental follow-up represents a critical gap, as the true measure of success for preterm birth prevention lies not only in reducing early delivery but also in ensuring optimal childhood outcomes. Future studies should incorporate extended follow-up assessments at 2–5 years to evaluate cognitive, motor, and behavioral development, aligning with recent recommendations from the NIH Task Force on preterm birth research priorities. These limitations highlight the need for multicenter randomized trials with prospective controls and standardised long-term outcome measures to confirm these findings and assess their broader applicability.

CONCLUSION

This study provides compelling evidence that a multimodal strategy combining antenatal corticosteroids (ACS), optimized prenatal care, and targeted infection management reduces preterm birth (PTB) rates by 44%, with particularly robust effects in high-risk subgroups such as women with a short cervix (<25 mm) and those at risk of early PTB (<34 weeks). The key clinical implications are clear: routine infection screening (including universal UTI testing and vaginal microbiome assessment) should be standard in high-risk pregnancies, given its significant contribution to reducing inflammation-driven PTB; frequent, risk-stratified prenatal visits enable early detection and intervention for emerging complications; and while ACS remains a cornerstone of PTB prevention, its efficacy is markedly enhanced when integrated with comprehensive care protocols. Moving forward, three critical research priorities emerge: First, cluster-randomized trials are needed to validate this model's effectiveness across diverse healthcare settings, particularly in rural or low-resource areas where implementation challenges may differ. Second, cost-effectiveness analyses in LMICs must evaluate scalability, as the economic burden of PTB is disproportionately borne by these regions. Third, advancing personalized prevention strategies—through biomarkers like cervicovaginal IL-6, fetal fibronectin, or metabolomic profiling—could refine risk stratification and allow tailored interventions. These steps would bridge the gap between efficacy trials and real-world impact, ultimately progressing toward the WHO's goal of reducing global PTB rates by 30% by 2030.

REFERENCES

1. Chawanpaiboon S, Vogel JP, Moller AB, et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. Lancet Glob Health. 2019;7(1):e37-e46.
2. Roberts D, Brown J, Medley N, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2017;3:CD004454.
3. Jobe AH, Goldenberg RL. Antenatal corticosteroids: an assessment of anticipated benefits and potential risks. Am J Obstet Gynecol. 2018;219(1):62-74.

4. Norman JE, Marlow N, Messow CM, et al. Vaginal progesterone prophylaxis for preterm birth (the OPPTIMUM study): a multicentre, randomised, double-blind trial. Lancet. 2016;387(10033):2106-2116.
5. Crowther CA, McKinlay CJ, Middleton P, Harding JE. Repeat doses of prenatal corticosteroids for women at risk of preterm birth for improving neonatal health outcomes. Cochrane Database Syst Rev. 2015;7:CD003935.
6. ACOG Committee Opinion No. 713: Antenatal corticosteroid therapy for fetal maturation. Obstet Gynecol. 2017;130(2):e102-e109.
7. Romero R, Dey SK, Fisher SJ. Preterm labor: one syndrome, many causes. Science. 2020;345(6198):760-765.
8. Henderson J, Carson C, Redshaw M. Impact of preterm birth on maternal well-being and women's perceptions of their baby: a population-based survey. JAMA Netw Open. 2022;5(3):e221770.
9. Keim SA, Pruitt NT. Gestational weight gain and child adiposity at age 3 years. Am J Obstet Gynecol. 2021;224(3):310.e1-310.e17.
10. Vogel JP, Souza JP, Gülmezoglu AM. Maternal complications and perinatal mortality: findings of the World Health Organization Multicountry Survey on Maternal and Newborn Health. Lancet Glob Health. 2023;11(1):e23-e33.
11. Brocklehurst P, Gordon A, Heatley E, Milan SJ. Antibiotics for treating bacterial vaginosis in pregnancy. Cochrane Database Syst Rev. 2013;1:CD000262.
12. Society for Maternal-Fetal Medicine (SMFM). Electronic address: pubs@smfm.org. SMFM Statement: Antibiotic prophylaxis for cesarean delivery. Am J Obstet Gynecol. 2022;226(6):B2-B8.
13. Conde-Agudelo A, Romero R. Predictive accuracy of changes in transvaginal sonographic cervical length over time for preterm birth: a systematic review and meta-analysis. Am J Obstet Gynecol. 2015;213(6):789-801.
14. Dodd JM, Jones L, Flenady V, et al. Prenatal administration of progesterone for preventing preterm birth in women considered to be at risk of preterm birth. Cochrane Database Syst Rev. 2013;7:CD004947.
15. Romero R, Nicolaides KH, Conde-Agudelo A, et al. Vaginal progesterone decreases preterm birth ≤34 weeks of gestation in women with a singleton pregnancy and a short cervix: an updated meta-analysis including data from the OPPTIMUM study. Ultrasound Obstet Gynecol. 2016;48(3):308-317.
16. Manuck TA, Esplin MS, Biggio J, et al. Predictors of response to 17-alpha hydroxyprogesterone caproate for prevention of recurrent preterm birth. Am J Obstet Gynecol. 2016;214(3):376.e1-376.e8.
17. Mercer BM, Egerman RS, Beazley DD, et al. Antibiotic therapy for reduction of infant morbidity after preterm premature rupture of the membranes: a randomized controlled trial. BMJ. 2021;372:n385.
18. Fonseca EB, Celik E, Parra M, et al. Progesterone and the risk of preterm birth among women with a short cervix. N Engl J Med. 2016;357(5):462-469.
19. WHO. Preterm birth fact sheet. 2023. Available from: https://www.who.int/news-room/fact-sheets/detail/preterm-birth.