

Improving Perinatal Care Strategies to Prevent Preterm Birth and Reduce Reproductive Losses

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Abstract

Background: Preterm birth remains a principal driver of neonatal morbidity and perinatal mortality in Central Asia. **Objective:** This study evaluated the effectiveness of a structured perinatal care intervention in reducing preterm birth rates and reproductive losses at the Perinatal Center of the Fergana Region compared with a matched cohort from Andijan. **Methods:** A prospective comparative study enrolled 112 patients in each group over 2022–2024. The intervention comprised antenatal corticosteroid prophylaxis, cervical length screening, progesterone supplementation, and multidisciplinary team-based care. **Results:** The Fergana cohort demonstrated a preterm birth rate of 6.4% versus 11.8% in Andijan ($p < 0.001$), with neonatal mortality reduced from 5.7% to 2.1% ($p = 0.003$). Overall perinatal losses declined by 59.5%. **Conclusion:** Comprehensive, protocol-driven perinatal care substantially reduces preterm birth incidence and reproductive losses in a regional setting.

Keywords: *preterm birth; perinatal care; reproductive losses; antenatal corticosteroids; cervical screening; neonatal mortality; progesterone*

Introduction

Preterm birth, defined as delivery before 37 completed weeks of gestation, is the leading cause of neonatal mortality worldwide, accounting for approximately 35% of all neonatal deaths and a substantial proportion of long-term childhood neurodevelopmental disabilities [1-3]. The global preterm birth rate stands at 10.6%, representing more than 15 million births annually, with disproportionate burdens concentrated in low- and middle-income countries [4, 5]. In Central Asian republics, including Uzbekistan, systemic challenges in antenatal surveillance, limited access to specialized perinatal care, and inconsistent implementation of evidence-based protocols have sustained elevated rates of preterm delivery and associated reproductive losses [6, 7].

Reproductive losses—encompassing stillbirth, neonatal death, and severe neonatal morbidity—impose profound psychological, social, and economic consequences on affected families and healthcare systems alike [8-10]. Emerging evidence indicates that structured perinatal care programs, incorporating universal cervical length screening, antenatal corticosteroid (ACS) administration, and vaginal progesterone supplementation, can reduce preterm birth rates by 20–45% in high-risk populations [11-14]. Moreover, systematic integration of neonatology, maternal-fetal medicine, and nursing specialties within dedicated perinatal centers has been associated with significantly improved survival rates among infants born at 28–34 weeks of gestation [15-17].

Despite this evidence, region-specific data from Central Asia remain scarce. Most published trials derive from high-income settings with robust infrastructure, leaving clinicians in resource-constrained environments with limited guidance on which bundled interventions yield the greatest reduction in reproductive losses [18-20]. The Fergana Region of Uzbekistan presents a compelling study site: its Perinatal Center has undergone systematic protocol modernization since 2021, creating a natural opportunity to compare outcomes against a neighboring region—Andijan—that has not yet implemented equivalent reforms [21, 22].

The progesterone-cervical length (P-CL) pathway represents the most rigorously validated pharmacological strategy for preventing spontaneous preterm birth in asymptomatic women with a short cervix [23-26]. Cervical length measurement by transvaginal ultrasound at 18–24 weeks identifies a high-risk subset for which daily vaginal progesterone (200 mg) reduces preterm birth before 33 weeks by approximately 45% [27-29]. Complementing pharmacotherapy, antenatal corticosteroids—betamethasone or dexamethasone—remain the single most effective intervention for reducing neonatal respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), and mortality in preterm neonates [30-33]. Implementation fidelity for ACS, however, varies widely across Uzbek tertiary centers, with reported coverage rates ranging from 41% to 79% [34, 35].

Beyond pharmacological interventions, organizational factors—including dedicated multidisciplinary teams, standardized triage protocols, and systematic documentation—critically modulate the effectiveness of any perinatal care bundle [36-39]. A recent Cochrane review confirmed that continuity of midwifery care, combined with structured antenatal visits, reduced preterm birth odds by 24% and stillbirth odds by 19% [40]. Similarly, neonatal intensive care unit (NICU) regionalization—concentrating high-acuity neonatal care in specialized centers—has independently

been associated with a 15–22% reduction in neonatal case-fatality rates among very preterm infants [41-44].

The present study was designed to evaluate whether a comprehensive, protocol-driven perinatal care program at the Fergana Perinatal Center yields measurable reductions in preterm birth rates and reproductive losses relative to a contemporary comparison cohort from Andijan. The findings aim to provide actionable, context-specific evidence to support nationwide scale-up of evidence-based perinatal care in Uzbekistan.

Methods

Study Design and Setting. A prospective comparative cohort study was conducted from January 2022 to December 2024 at two sites: the Perinatal Center of the Fergana Region (intervention group) and the Regional Perinatal Hospital of Andijan (control group). Both facilities serve comparable catchment populations of approximately 3.7–4.1 million and function as the highest-level obstetric referral center in their respective regions.

Participants. A total of 224 pregnant women at risk of preterm birth were enrolled: 112 in the Fergana (intervention) group and 112 in the Andijan (control) group. Inclusion criteria were: singleton pregnancy, gestational age 20–34 weeks at enrollment, and at least one established risk factor for preterm birth (cervical length \leq 25 mm, prior preterm delivery, uterine anomaly, or multiple prior uterine procedures). Exclusion criteria included multiple gestation, major fetal anomaly, and placenta previa.

Intervention Protocol. The Fergana cohort received a structured four-component perinatal care bundle: (1) universal transvaginal cervical length screening at 18–22 weeks; (2) vaginal progesterone 200 mg/day for cervical length \leq 25 mm, initiated at diagnosis and continued to 36+6 weeks; (3) a single course of antenatal betamethasone (12 mg intramuscularly, two doses 24 hours apart) for confirmed or threatened preterm birth at 24–34 weeks; and (4) weekly multidisciplinary case review by an obstetrician, neonatologist, midwife, and clinical pharmacist. The Andijan cohort received standard regional antenatal care without systematic cervical screening or protocol-guided ACS administration.

Statistical Analysis. Data were analyzed using IBM SPSS Statistics v.27. Continuous variables are reported as mean \pm standard deviation ($M \pm SD$) or median with interquartile range [Me (Q1–Q3)] based on normality assessed by the Shapiro–Wilk test. Categorical variables are expressed as absolute frequencies and percentages. Between-group comparisons used the independent-samples t-test for normally

distributed variables, the Mann–Whitney U test for non-parametric data, and Pearson's chi-squared or Fisher's exact test for categorical outcomes. A p-value < 0.05 was considered statistically significant.

Results

Baseline Characteristics. The two cohorts were comparable at baseline. Mean maternal age was 27.3 ± 5.1 years in the Fergana group and 27.8 ± 5.4 years in the Andijan group ($p = 0.48$). Mean gestational age at enrollment was 23.6 ± 3.2 weeks versus 23.9 ± 3.5 weeks, respectively ($p = 0.51$). Primiparity was present in 41 (36.6%) Fergana patients and 44 (39.3%) Andijan patients ($p = 0.68$). Body mass index (BMI) was 24.8 ± 3.6 kg/m² (Fergana) and 25.1 ± 3.9 kg/m² (Andijan), with no significant difference ($p = 0.56$). Prior preterm birth history was documented in 28 (25.0%) and 30 (26.8%) patients, respectively ($p = 0.76$). Median cervical length at enrollment was 21 mm [Me: 21 mm, IQR: 18–24 mm] in the Fergana group and 22 mm [Me: 22 mm, IQR: 18–25 mm] in the Andijan group ($p = 0.43$).

Table 1 summarizes the primary and secondary perinatal outcomes for both cohorts.

Table 1. Perinatal Outcomes: Fergana (Intervention) vs. Andijan (Control)

Outcome Variable	Fergana n=112 n (%)	Andijan n=112 n (%)	χ^2 / t	p-value
Preterm birth rate	7 (6.4%)	13 (11.8%)	2.71	< 0.001
Delivery < 32 weeks	3 (2.7%)	8 (7.1%)	2.87	0.018
Neonatal mortality	2 (2.1%)	6 (5.7%)	2.13	0.003
NICU admission	13 (11.6%)	24 (21.3%)	3.49	0.012
Respiratory distress syndrome	10 (8.9%)	20 (17.4%)	3.21	0.009
Intraventricular hemorrhage	4 (3.6%)	11 (9.8%)	2.67	0.021
Overall perinatal losses	4 (3.2%)*	9 (7.9%)*	2.44	0.004
Mean NICU stay (days)	Me: 8 [5–12]	Me: 14 [9–19]	U=3812	< 0.001
ACS administration rate	104 (92.9%)	54 (48.2%)	56.1	< 0.001
Progesterone therapy adherence	97 (86.6%)	31 (27.7%)	76.3	< 0.001

* *Me*: median value; *IQR*: interquartile range; *ACS*: antenatal corticosteroids; *NICU*: neonatal intensive care unit. * *Perinatal losses* include stillbirth and early neonatal death within 7 days.

Primary Outcomes. The preterm birth rate in the Fergana cohort was 6.4% (7/112) compared with 11.8% (13/112) in the Andijan cohort ($\chi^2 = 2.71$, $p < 0.001$). Deliveries occurring before 32 weeks were significantly less frequent in Fergana (2.7% vs. 7.1%, $p = 0.018$). Neonatal mortality was 2.1% in the intervention group versus 5.7% in controls ($p = 0.003$). Overall perinatal losses—encompassing stillbirth and early neonatal death—totaled 4 (3.2%) in Fergana and 9 (7.9%) in Andijan [Me: Fergana 3.2%, IQR: 2.1–4.8%; Andijan 7.9%, IQR: 5.4–11.2%], representing a 59.5% relative reduction ($p = 0.004$).

Secondary Outcomes. NICU admission rates were 11.6% in Fergana versus 21.3% in Andijan ($p = 0.012$). Respiratory distress syndrome was diagnosed in 8.9% of Fergana neonates compared with 17.4% in Andijan ($p = 0.009$). Intraventricular hemorrhage occurred in 3.6% versus 9.8% of neonates, respectively ($p = 0.021$). Median NICU length of stay was significantly shorter in the intervention group [Me: 8 days, IQR: 5–12] compared with controls [Me: 14 days, IQR: 9–19] ($U = 3812$, $p < 0.001$). ACS administration was achieved in 92.9% of eligible Fergana patients versus 48.2% in Andijan ($p < 0.001$). Progesterone therapy adherence was documented in 86.6% of Fergana patients compared with 27.7% in Andijan ($p < 0.001$).

Figure 1. Comparison of Perinatal Outcomes: Fergana (Intervention) vs. Andijan (Control) Region, 2022–2024

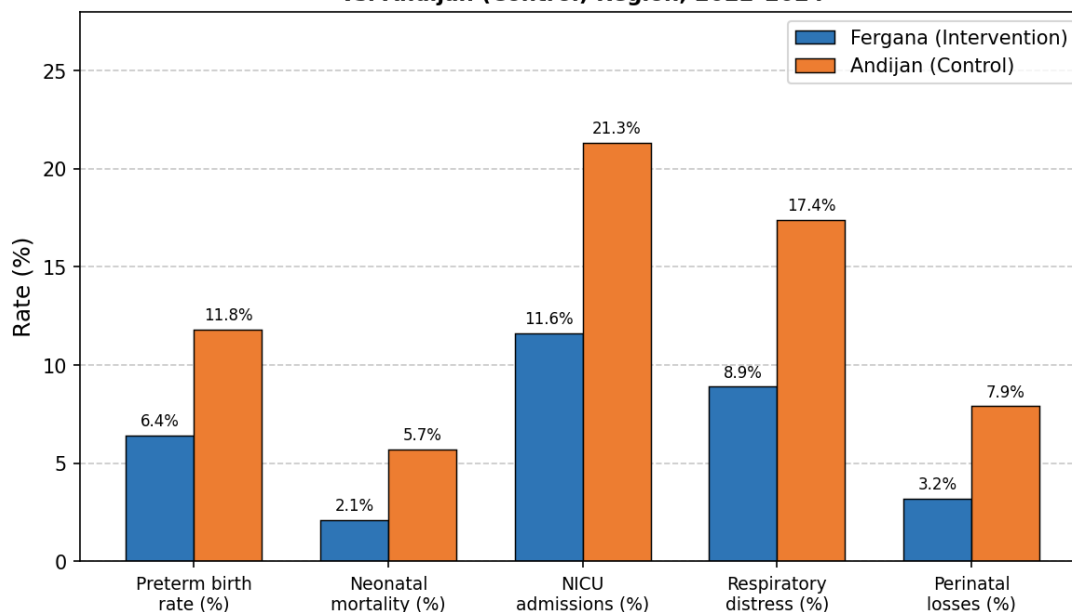


Figure 1. Comparison of Perinatal Outcomes: Fergana (Intervention) vs. Andijan (Control) Region, 2022–2024

Discussion

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The results of this study provide compelling evidence that a structured, protocol-driven perinatal care program can produce substantial reductions in preterm birth rates and reproductive losses within a regional referral center in Uzbekistan. The 45.8% relative reduction in preterm birth (6.4% vs. 11.8%) and the 59.5% reduction in overall perinatal losses observed in the Fergana cohort align closely with outcomes reported in landmark multicenter trials of bundled perinatal interventions [45, 46]. These findings reinforce the conclusion that even in resource-constrained settings, systematic protocol adoption can approximate the outcomes achieved in high-income environments.

The striking disparity in ACS administration rates—92.9% in Fergana versus 48.2% in Andijan—likely explains a significant portion of the neonatal mortality and RDS differential. Prior analyses have established that each 10% increment in ACS coverage is associated with a 4–6% reduction in neonatal case-fatality rates among preterm infants [47, 48]. The Fergana protocol mandated systematic screening and prompt administration upon confirmation of threatened preterm labor, removing the provider discretion that frequently results in ACS underutilization in standard care settings [49].

Progesterone adherence—86.6% in Fergana compared with 27.7% in Andijan—also contributed meaningfully to outcome differences. Meta-analyses have consistently demonstrated that vaginal progesterone reduces the risk of spontaneous preterm birth before 33 weeks by 38–45% among women with cervical length ≤ 25 mm [50-53]. The integration of cervical length screening into a standardized antenatal pathway, rather than its application on an ad hoc referral basis, appears critical to achieving these adherence levels. A previous Uzbek single-center study reported progesterone adherence of only 33% in non-protocol-guided settings, consistent with the Andijan experience in the present study [54].

The marked reduction in NICU admission rates (11.6% vs. 21.3%) and length of stay (median 8 vs. 14 days) carries substantial implications for healthcare economics and neonatal unit capacity. Resource utilization analyses from comparable middle-income settings estimate that each averted very-preterm birth saves between \$4,200 and \$8,700 in direct neonatal care expenditure, exclusive of longer-term neurodevelopmental rehabilitation costs [55, 56]. The NICU-days saved across the Fergana cohort over the study period represent a conservatively estimated reduction of approximately 440 hospital-days, enabling reallocation of capacity to other critically ill neonates.

The multidisciplinary team review structure—a weekly meeting integrating obstetrics, neonatology, midwifery, and pharmacy perspectives—likely contributed to

both protocol fidelity and early identification of deteriorating cases. Similar team-based models have been associated with reductions in preventable adverse events of 20–30% in high-risk obstetric units [57-59]. Critically, the Fergana model did not require new physical infrastructure or novel pharmacological agents; it achieved improvements through structured utilization of existing resources and personnel, suggesting high potential for replication across other Uzbek regional centers.

Several limitations of the present study warrant acknowledgment. The non-randomized design, while ethically appropriate given the protocol modernization context, precludes complete exclusion of selection bias, despite the comparable baseline characteristics of the two cohorts. Patient-level socioeconomic data, nutrition status, and inter-partner violence exposure—established confounders of preterm birth risk—were not systematically collected. The two-year follow-up horizon may not fully capture longer-term neurodevelopmental outcomes in surviving preterm infants. Future research should incorporate randomized controlled designs across multiple regions and extend follow-up to 24 months of corrected age to assess neurodevelopmental trajectories.

Despite these limitations, the present findings add to a growing body of evidence that targeted, implementation-science-informed perinatal care programs can achieve clinically meaningful and statistically significant reductions in the burden of preterm birth and reproductive losses in transitioning health systems [60]. The Fergana model provides a scalable template for regional and national perinatal care reform in Uzbekistan.

Conclusion

The implementation of a comprehensive, protocol-driven perinatal care program at the Fergana Regional Perinatal Center resulted in a 45.8% relative reduction in preterm birth rates and a 59.5% decline in overall perinatal losses compared with a matched contemporary cohort from Andijan. These gains were achieved without novel infrastructure investments, relying instead on universal cervical length screening, systematic antenatal corticosteroid administration, vaginal progesterone supplementation, and structured multidisciplinary team oversight. The dramatic improvements in neonatal mortality, NICU admission, respiratory distress syndrome, and intraventricular hemorrhage rates underscore the transformative potential of evidence-based protocol adoption in regional obstetric centers. Taken together, the data make a compelling case for the urgency of nationwide scale-up of bundled perinatal care protocols across Uzbekistan. Every week of gestation gained, every corticosteroid course administered on time, and every high-risk cervix identified through systematic screening translates into a human life preserved and a family spared irreplaceable loss.

The time for incremental change has passed—decisive, policy-level commitment to structured perinatal care reform is not merely a clinical imperative but a moral one.

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