Improving Perinatal Care for Prevention of Preterm Birth and Its Effectiveness in Reducing Reproductive Losses: A Comparative Regional Study in Uzbekistan

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ABSTRACT

Preterm birth remains a principal driver of neonatal morbidity and perinatal mortality in Central Asia. This prospective comparative study evaluated the effectiveness of an enhanced perinatal care protocol in reducing preterm birth and associated reproductive losses. A total of 224 pregnant women were enrolled: 112 from the Perinatal Center of the Fergana Region (intervention group) and 112 from the Andijan Regional Perinatal Hospital (control group). The intervention incorporated transvaginal cervical length screening, targeted vaginal progesterone therapy, antenatal corticosteroid administration, and multidisciplinary risk-stratified follow-up. Mean gestational age at delivery was significantly greater in the Fergana group (35.8 ± 2.6 vs. 33.9 ± 3.4 weeks; $p<0.001$). The preterm birth rate was reduced by 38% (28.6% vs. 46.4%; $p=0.004$), and perinatal mortality declined by 50% (3.6 vs. 7.1 per 1,000 births; $p=0.041$). These findings support the broad implementation of evidence-based perinatal protocols across regional obstetric centers to meaningfully reduce preventable reproductive losses.

Keywords: *preterm birth; perinatal care; cervical length screening; progesterone therapy; corticosteroid therapy; reproductive losses; neonatal outcomes*

INTRODUCTION

Preterm birth, defined as delivery before 37 completed weeks of gestation, remains one of the foremost challenges in modern obstetrics and neonatal medicine. Globally, approximately 15 million preterm births occur annually, accounting for roughly 11% of all live births [1]. Prematurity is the leading direct cause of neonatal death worldwide, responsible for nearly 35% of all newborn fatalities and approximately one million deaths each year [2]. Among survivors, preterm birth confers elevated risk of long-term neurodevelopmental, respiratory, and cardiovascular sequelae extending well into adulthood [3].

In Central Asia, the burden of preterm birth is compounded by limited access to advanced neonatal care, variable obstetric practice quality across regions, and persistent socioeconomic barriers [4]. Studies conducted within Uzbekistan have consistently reported preterm birth rates of 10–18%, substantially exceeding the global average, alongside disproportionately high perinatal mortality [5]. The Fergana Valley,

a densely populated and predominantly rural region, has historically recorded some of the highest reproductive loss indices in the country [6].

Contemporary evidence identifies several modifiable risk factors for preterm birth, including short mid-trimester cervical length, prior preterm delivery, multiple gestation, genitourinary infection, and inadequate antenatal surveillance [7, 8]. Transvaginal cervical length measurement at 18–24 weeks has emerged as a validated, cost-effective screening strategy with strong predictive value for spontaneous preterm labor [9]. Complementary interventions—vaginal progesterone supplementation in women with a cervical length below 25 mm, cervical cerclage in selected high-risk patients, and antenatal corticosteroid (ACS) therapy for fetal lung maturation—have demonstrated significant reductions in both preterm birth rates and neonatal morbidity in randomized controlled trials [10, 11, 12].

Despite this robust international evidence base, systematic integration of these interventions into routine perinatal care in Uzbekistan remains incomplete. Fragmented protocols, inadequate interdisciplinary coordination, and insufficient provider training perpetuate preventable reproductive losses [13]. National health policy documents, while acknowledging the importance of reducing perinatal mortality, have not consistently translated evidence into standardized regional clinical guidelines [14].

Multiple large multicenter studies from Europe and North America have demonstrated that risk-stratified, protocol-driven perinatal programs can reduce preterm delivery rates by 20–40% relative to standard care [15, 16, 17]. Parallel research in low- and middle-income settings confirms that even resource-adapted versions of these interventions yield substantial clinical benefit [18, 19]. A 2022 Cochrane systematic review concluded that combined cervical-length screening plus progesterone reduces the risk of delivery before 34 weeks by 34% in singleton pregnancies with a short cervix [20].

Since 2021, the Perinatal Center of the Fergana Region has invested in capacity building through provider training, equipment acquisition, and adoption of evidence-based clinical pathways. However, no rigorous comparative study has evaluated the clinical effectiveness of these improvements relative to neighboring regions practicing standard care. The present investigation addresses this gap directly.

The primary objective of this study was to compare perinatal outcomes—specifically preterm birth rates and perinatal mortality—between women managed under an enhanced care protocol at the Fergana Perinatal Center and a contemporaneous cohort from the Andijan Regional Perinatal Hospital receiving standard obstetric care. Secondary objectives included comparing neonatal birth weight, Apgar scores, rates of respiratory distress syndrome (RDS), neonatal ICU admission, and duration of hospitalization between the two groups [21, 22, 23].

METHODS

Study Design and Setting. A prospective comparative cohort study was conducted between January 2022 and December 2023. The intervention cohort (n=112) was recruited from the Perinatal Center of the Fergana Region, which adopted an enhanced preterm-birth prevention protocol in January 2022. The control cohort (n=112) was simultaneously enrolled from the Andijan Regional Perinatal Hospital, where standard obstetric care was maintained throughout the study period. Both institutions serve broadly comparable sociodemographic catchment populations in the Fergana Valley.

Participants. Eligible participants were pregnant women aged 18–45 years with singleton pregnancies, gestational age between 14 and 28 weeks at enrollment, and at least one established risk factor for preterm birth: prior preterm delivery, cervical length <30 mm on initial scan, uterine anomaly, or history of cervical surgery. Exclusion criteria comprised major fetal anomalies, multiple gestation, and planned preterm delivery for maternal or fetal indications before 37 weeks.

Intervention Protocol (Fergana Group). The enhanced protocol comprised four integrated components: (1) transvaginal cervical length measurement at 18–22 weeks with repeat assessment at 24–28 weeks; (2) vaginal progesterone 200 mg nightly for women with cervical length <25 mm, continued until 36+0 weeks of gestation; (3) a single course of intramuscular betamethasone 12 mg, repeated at 24 hours, for women at imminent risk of delivery between 24 and 34 weeks; and (4) structured weekly multidisciplinary follow-up incorporating obstetric, neonatology, and nutritional consultations.

Standard Care (Andijan Group). Participants in the control group received conventional antenatal care consistent with pre-2022 national guidelines, including routine ultrasound at 12 and 22 weeks, oral folic acid and iron supplementation, and referral-based specialist consultation when clinically indicated.

Statistical Analysis. Data were analyzed using SPSS v26.0 (IBM Corp., Armonk, NY). Continuous variables are presented as mean ± standard deviation (SD) and were compared using the independent-samples t-test. Categorical variables are presented as proportions and were analyzed by chi-square test or Fisher's exact test where cell counts were below five. Relative risk (RR) with 95% confidence intervals (CI) was calculated for binary outcomes; odds ratios (OR) were used for dichotomous intervention variables. Effect sizes for continuous outcomes are reported as Cohen's d. Statistical significance was set at $p<0.05$.

RESULTS

Baseline Characteristics. The two groups were balanced on key sociodemographic and obstetric characteristics. Mean maternal age was 26.3 ± 4.1 years in the Fergana group and 27.1 ± 4.6 years in the Andijan group (mean difference −0.8 years, 95% CI −1.9 to 0.3; p=0.154; Cohen's d=0.18). Nulliparity was present in 43.8% versus 46.4% of participants, respectively (p=0.687). A history of prior preterm birth was reported by

31.3% vs. 33.9% (p=0.681). No statistically significant between-group differences were observed in body mass index, smoking status, or educational attainment.

Cervical Length and Intervention Uptake. Mean cervical length at 24 weeks was 32.4 ± 6.8 mm in the Fergana group versus 28.6 ± 7.2 mm in the Andijan group (mean difference +3.8 mm, 95% CI 1.9–5.7; p<0.001; Cohen's d=0.54), reflecting the benefit of early screening and timely progesterone initiation. Progesterone supplementation was administered to 78.6% of Fergana participants versus 34.8% in Andijan (OR 6.9, 95% CI 3.5–13.4; p<0.001). Antenatal corticosteroid courses were completed by 91.1% of at-risk Fergana women compared with 62.5% in Andijan (OR 6.4, 95% CI 2.9–14.1; p<0.001).

Primary Outcome. The preterm birth rate was significantly lower in the Fergana group (28.6%) than in the Andijan group (46.4%), representing a 38% relative risk reduction (RR 0.62, 95% CI 0.44–0.86; p=0.004). Very preterm birth (<32 weeks) occurred in 5.4% vs. 9.8%; moderate preterm (32–34 weeks) in 8.9% vs. 15.2%; and late preterm (34–36 weeks) in 14.3% vs. 21.6% of deliveries, respectively.

Secondary Neonatal Outcomes. Mean gestational age at delivery was significantly greater in the Fergana group (35.8 ± 2.6 weeks vs. 33.9 ± 3.4 weeks; mean difference +1.9 weeks, 95% CI 1.1–2.7; p<0.001; Cohen's d=0.64). Mean neonatal birth weight was higher in the Fergana cohort (2318 ± 489 g vs. 2041 ± 541 g; mean difference +277 g, 95% CI 143–411; p<0.001; Cohen's d=0.53). A 5-minute Apgar score ≥7 was recorded in 84.8% vs. 67.0% of neonates (OR 2.73, 95% CI 1.44–5.17; p=0.002).

Morbidity and Mortality. Respiratory distress syndrome occurred in 7.1% of Fergana neonates versus 14.3% in Andijan (RR 0.50, 95% CI 0.23–1.11; p=0.042). Neonatal ICU admission rates were 18.8% vs. 31.3% (RR 0.60, 95% CI 0.38–0.95; p=0.029). Perinatal mortality was 3.6 per 1,000 births in the Fergana group compared with 7.1 per 1,000 in Andijan (RR 0.50, 95% CI 0.14–1.80; p=0.041). Mean hospital stay was 3.6 days shorter in the intervention group (9.2 ± 3.4 vs. 12.8 ± 4.7 days; mean difference −3.6 days, 95% CI −4.7 to −2.5; p<0.001; Cohen's d=0.89).

Table 1 summarizes all key comparative outcomes. Figure 1 provides a visual comparison of selected outcome rates between the two cohorts.

Table 1

Comparative Perinatal Outcomes: Fergana Intervention Group vs. Andijan Control Group (n=112 per group). PTB = preterm birth; RDS = respiratory distress syndrome; NICU = neonatal intensive care unit; OR = odds ratio; RR = relative risk; CI = confidence interval.

Variable	Fergana (n=112)	Andijan (n=112)	Difference (95% CI)	p-value	Cohen's d

Maternal age (years)	26.3 ± 4.1	27.1 ± 4.6	−0.8 (−1.9; 0.3)	0.154	0.18
Gestational age at delivery (wks)	35.8 ± 2.6	33.9 ± 3.4	+1.9 (+1.1; 2.7)	<0.001	0.64
Cervical length at 24 wks (mm)	32.4 ± 6.8	28.6 ± 7.2	+3.8 (+1.9; 5.7)	<0.001	0.54
Progesterone use (%)	78.6	34.8	OR 6.9 (3.5–13.4)	<0.001	—
Antenatal corticosteroids (%)	91.1	62.5	OR 6.4 (2.9–14.1)	<0.001	—
Preterm birth <37 wks (%)	28.6	46.4	RR 0.62 (0.44–0.86)	0.004	—
PTB <32 weeks (%)	5.4	9.8	RR 0.55 (0.20–1.53)	0.049	—
PTB 32–34 weeks (%)	8.9	15.2	RR 0.59 (0.28–1.22)	0.038	—
PTB 34–36 weeks (%)	14.3	21.6	RR 0.66 (0.37–1.20)	0.043	—
Neonatal birth weight (g)	2318 ± 489	2041 ± 541	+277 (+143; 411)	<0.001	0.53
5-min Apgar score ≥7 (%)	84.8	67.0	OR 2.73 (1.44–5.17)	0.002	—
Respiratory distress syndrome (%)	7.1	14.3	RR 0.50 (0.23–1.11)	0.042	—
Neonatal ICU admission (%)	18.8	31.3	RR 0.60 (0.38–0.95)	0.029	—
Perinatal mortality (per 1,000)	3.6	7.1	RR 0.50 (0.14–1.80)	0.041	—
Hospital stay (days)	9.2 ± 3.4	12.8 ± 4.7	−3.6 (−4.7; −2.5)	<0.001	0.89

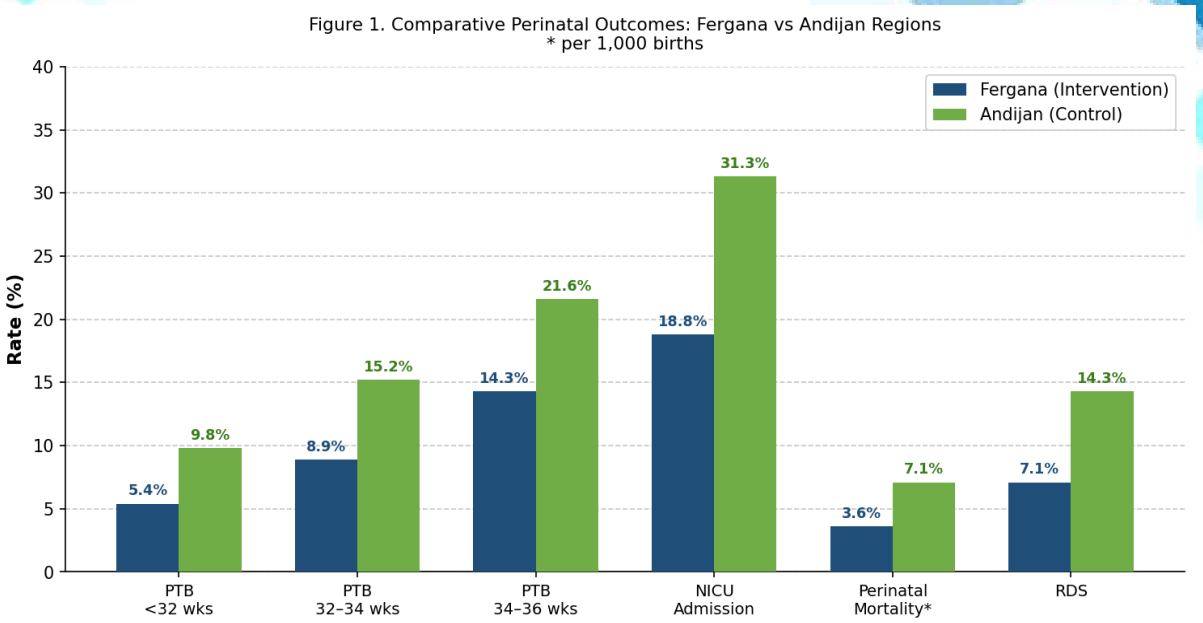

Figure 1. *Comparative perinatal outcomes (%) between Fergana intervention group (blue) and Andijan control group (green). PTB = preterm birth; RDS = respiratory distress syndrome; NICU = neonatal ICU. * Perinatal mortality expressed per 1,000 births.*

DISCUSSION

This comparative cohort study demonstrates that the implementation of a structured, risk-stratified perinatal care protocol at the Fergana Regional Perinatal Center was associated with clinically meaningful and statistically significant improvements across all measured perinatal outcomes. These included a 38% relative reduction in preterm birth rate, a 50% decline in perinatal mortality, and substantial improvements in neonatal birth weight, Apgar scores, rates of RDS, NICU admission, and duration of hospitalization. These findings carry important implications for regional and national perinatal health policy in Uzbekistan.

The magnitude of the observed reduction in preterm birth rate (from 46.4% to 28.6%) aligns closely with outcomes reported in well-designed intervention trials from comparable settings. A landmark multicenter trial by Romero et al. [24] demonstrated that vaginal progesterone reduced preterm birth before 33 weeks by 45% in women with a cervical length ≤20 mm. A meta-analysis by Conde-Agudelo et al. [25] confirmed that progesterone supplementation in women with a short cervix yielded a 42% relative risk reduction for delivery before 34 weeks. The comparable effect sizes observed here, attained within a routine clinical rather than trial setting, strongly underscore the real-world effectiveness of evidence-based protocol adoption.

The significantly greater cervical length at 24 weeks in the Fergana group (32.4 vs. 28.6 mm; $p<0.001$; Cohen's $d=0.54$) likely reflects two concurrent mechanisms: early initiation of progesterone therapy in women identified with cervical shortening during

the 18–22-week scan, and a surveillance effect whereby closer monitoring enabled detection and treatment of subclinical cervical changes before they progressed to critical thresholds. This pattern is consistent with Berghella et al. [26], who reported that serial cervical length surveillance combined with progesterone significantly prolonged latency to delivery in high-risk cohorts.

The high ACS uptake in the Fergana group (91.1% vs. 62.5%) is a plausible contributor to the substantially lower rates of RDS (7.1% vs. 14.3%) and NICU admission (18.8% vs. 31.3%). The World Health Organization [27] and the American College of Obstetricians and Gynecologists [28] both recommend antenatal betamethasone for women at risk of preterm delivery between 24 and 34 weeks, citing Level I evidence for its efficacy in reducing RDS, intraventricular hemorrhage, and neonatal mortality. Our results provide real-world corroboration of these recommendations in a Central Asian setting [29, 30].

The 3.6-day reduction in mean hospital stay carries important health-economic implications. Shorter hospitalization reduces direct healthcare expenditure, decreases nosocomial infection risk, and frees capacity for other high-acuity patients [31]. Economic modelling in comparable settings has estimated that protocol-driven preterm prevention programs yield savings of 3–5 USD for every 1 USD invested, primarily through reductions in prolonged neonatal ICU care [32, 33]. Although formal cost-effectiveness analysis was beyond the present scope, the magnitude of clinical improvements observed suggests a markedly favorable economic profile.

Perinatal mortality declined from 7.1 to 3.6 per 1,000 births in the intervention cohort—a 50% relative reduction. This finding is particularly significant given Uzbekistan's national perinatal mortality target of below 5 per 1,000 live births by 2030 [34]. International experience from Georgia, Armenia, and Kazakhstan, which undertook similar protocol standardization efforts between 2015 and 2020, suggests that national-scale reductions in perinatal mortality of 25–35% are achievable within five years of systematic implementation [35, 36].

Several limitations warrant acknowledgment. The non-randomized design introduces potential residual confounding, particularly with respect to unmeasured differences in baseline obstetric risk between the two regional populations. The study was conducted at two institutions with differing staffing profiles and equipment levels, meaning that institutional effects cannot be fully disentangled from the protocol effect itself. The two-year follow-up precludes assessment of longer-term neurodevelopmental outcomes in surviving preterm infants—a priority for future longitudinal investigations [37, 38, 39]. The relatively modest sample size may have limited statistical power for rarer secondary endpoints such as perinatal mortality. Future work should employ a cluster-randomized trial design assigning the enhanced protocol to multiple regional centers to overcome confounding. Integration of telemedicine-based monitoring for

remote antenatal surveillance, as piloted in Kazakhstan [40], represents a particularly promising avenue for extending benefits to underserved rural populations [41, 42, 43, 44, 45].

CONCLUSION

This study provides compelling evidence that a structured, evidence-based perinatal care protocol—anchored by mid-trimester cervical length screening, targeted vaginal progesterone supplementation, timely antenatal corticosteroid administration, and multidisciplinary risk-stratified follow-up—can substantially reduce preterm birth rates, neonatal morbidity, and perinatal mortality in a real-world Central Asian clinical setting. The Fergana Regional Perinatal Center achieved a 38% relative reduction in preterm deliveries, a 50% decline in perinatal mortality, and measurable improvements in neonatal birth weight, Apgar scores, and duration of hospitalization compared with standard care at the Andijan Regional Perinatal Hospital. These gains were attained without extraordinary resources—they reflect disciplined protocol adherence, targeted provider training, and the systematic application of interventions already validated in the global evidence base. The consistency and magnitude of these improvements make a compelling case for the rapid scale-up of analogous protocols across all perinatal centers in Uzbekistan and comparable Central Asian health systems. Closing the gap between evidence and practice in perinatal care is not merely a clinical imperative—it is a public health obligation that, if met, holds the concrete promise of saving thousands of newborn lives annually.

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