https://doi.org/10.48047/AFJBS.6.15.2024.11576-11584

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

A Controlled Trial of Antepartum Glucocorticoid Treatment for Prevention of Respiratory Distress Syndrome in Premature Infants: A Cross-Sectional Study

Dr Sumera Qayyum[1*], Dr Amna Ihsan[2], Dr Henna Salman[3], Dr Ommia Kalsoom[4], Dr Danyal Khattak[5], Dr Syeda Maryam Batool[6]

[1*]Specialist Gynaecologist and Obstetrician, Central Clinic, Abu Dhabi
[2]Assistant Professor, Department of Biochemistry, King Edward Medical University, Lahore, Pakistan
[3]Associate Professor, Department of Physiology, Khyber Medical College, Peshawar, Pakistan
[4]Assistant Professor, Department of Physiology, Women Medical College, Abbottabad, Pakistan
[5]Demonstrator, Department of Physiology, KMU-IDS, Kohat, Pakistan
[6]Associate Professor, Department of Gynaecology and Obstetrics, Poonch Medical College/ SKBZ-CMH, Rawlakot, AJK

***Corresponding author's** email address: sumeramajid339@gmail.com

Volume 6, Issue 15, Sep 2024

Received: 15 July 2024

Accepted: 25 Aug 2024

Published: 25 Sep 2024

doi: 10.48047/AFJBS.6.15.2024.11576-11584

ABSTRACT

Background: Respiratory distress syndrome (RDS) remains a leading cause of morbidity and mortality among preterm infants. Antepartum glucocorticoid therapy is widely used to enhance fetal lung maturation and reduce the risk of RDS in premature newborns. This study evaluates the efficacy of glucocorticoid therapy in preventing RDS, examining key maternal, neonatal, and metabolic variables

Methodology: A cross-sectional, controlled clinical trial was conducted at Khyber Medical University from January 2023 to January 2024. A total of 101 preterm infants born between 28-34 weeks of gestation were included, divided into two groups: those whose mothers received glucocorticoid therapy (n=50) and a control group without treatment (n=51). Maternal hormonal levels, neonatal respiratory outcomes, and metabolic parameters were measured. 'Statistical analysis was conducted using Chi-square tests'.

Results: 'The incidence of RDS was significantly lower in the glucocorticoid group (12%) compared to the control group (35%) (p=0.008)'. The glucocorticoid group also demonstrated significantly higher lecithin/sphingomyelin ratios ($p<0.001$) and neonatal surfactant levels ($p<0.001$), alongside improved maternal hormonal profiles. Neonatal metabolic outcomes, including blood glucose and calcium levels, were more favorable i glucocorticoid group, with a notable reduction in hypoglycemia (p value 0.002), hypocalcemia (p value 0.04). Neonatal ICU admissions and the duration of NICU stay were also significantly reduced in the treatment group ($p<0.001$).

Conclusion: Antepartum glucocorticoid therapy significantly reduces the risk of RDS and improves neonatal respiratory and metabolic outcomes in preterm infants. These findings support the routine use of glucocorticoid therapy in managing pregnancies at risk of preterm delivery to improve neonatal health and reduce complications associated with prematurity.

Keywords: Antepartum Glucocorticoid, Respiratory Distress Syndrome, Premature Infants, newborns

Introduction

Respiratory distress syndrome (RDS) is a major complication in premature infants, primarily due to the immaturity of the lungs and insufficient production of surfactant. This condition leads to significant respiratory difficulty and, in severe cases, neonatal death (1). Advances in neonatal care have improved survival rates, but the prevention of RDS remains a priority in obstetric management, especially for preterm deliveries (2, 3).

A key intervention for preventing RDS is the administration of antepartum glucocorticoids (4). This therapy has been shown to stimulate fetal lung maturation by accelerating surfactant production and improving lung function. Studies and subsequent research confirmed that the use of corticosteroids before delivery significantly reduces the incidene and severity of RDS in preterm infants (3) .

This study investigates the efficacy of antepartum glucocorticoid therapy in preventing RDS among preterm infants, particularly in a controlled clinical setting at Khyber Medical University. It also assesses the associated physiological and biochemical changes in the mother and fetus.

Despite the widespread use of glucocorticoids in obstetric practice, there is still variation in outcomes based on gestational age, timing of administration, and maternal health factors. This study aims to provide further insight into these aspects, with an emphasis on how glucocorticoid therapy affects fetal development and neonatal outcomes within a well-defined clinical framework.

‘The prevention of respiratory distress syndrome is critical in reducing neonatal morbidity and mortality, particularly in preterm infants’. Previous studies have established that antenatal glucocorticoids can enhance fetal lung maturity, yet there are still gaps in understanding how various physiological and biochemical factors contribute to the overall efficacy of the treatment. This study addresses those gaps by evaluating the effects of glucocorticoid therapy in relation to maternal gynecological factors, fetal physiological responses, and biochemical markers.

Moreover, the study’s location at Khyber Medical University Peshawar offers a unique opportunity to analyze regional differences in outcomes, as variations in prenatal care practices and maternal health conditions may influence the treatment's success. The controlled setting of this trial ensures that these variables were carefully monitored, allowing for a more comprehensive assessment of the intervention's benefits.

Finally, this study contributes to the global effort to optimize antenatal care protocols by offering evidence-based recommendations for the use of glucocorticoids in high-risk pregnancies. The findings were expected to support healthcare providers in making informed decisions about the management of preterm births, ultimately improving neonatal outcomes.

Methodology

This was a cross-sectional, controlled clinical trial conducted at Khyber Medical University, Peshawar, from January 2023 to January 2024. The study aimed to evaluate the effectiveness of antepartum glucocorticoid therapy in preventing RDS in preterm infants. Participants were preterm infants born between 28-34 weeks of gestation. Mothers were divided into two groups: the intervention group, which received glucocorticoid therapy, and a control group that did not receive the treatment. Gynecological, physiological, and biochemical data were collected to

assess maternal health, fetal lung maturity, and neonatal outcomes. Ethical clearance for the study was obtained from the Institutional Review Board of Khyber Medical University. 'Written informed consent was obtained from all participating mothers'.

Inclusion Criteria Pregnant women with a gestational age between 28-34 weeks, Mothers at risk of preterm delivery, Singleton pregnancies. Exclusion Criteria: Multiple pregnancies, Fetal congenital anomalies, Maternal comorbidities affecting pregnancy outcomes.

Data were collected through clinical assessments, laboratory analyses, and neonatal outcomes recorded post-delivery. Maternal hormone levels, fetal lung maturity markers (including surfactant levels), and neonatal respiratory function were key variables of interest. Maternal serum samples were analyzed for hormone levels related to fetal development, including estrogen and progesterone. Fetal lung maturity was assessed through amniotic fluid lecithin/sphingomyelin ratios. Neonatal outcomes, such as Apgar scores and incidence of RDS, were recorded within the first 72 hours after birth.

Data were analyzed using SPSS. 'The Chi-square test was used to compare categorical variables, while logistic regression was performed to evaluate the association between glucocorticoid therapy and RDS outcomes'. 'A p-value of less than 0.05 was considered statistically significant'.

Results

Table 1 demographic characteristics of mothers and infants the average maternal age was similar between both groups, with no statistically significant difference (p=0.71). This suggests that age was not a confounding factor affecting neonatal outcomes. There was no significant difference in the mean gestational age between the glucocorticoid and control groups (p=0.29). Both groups had similar gestational profiles, ensuring comparability. Parity was evenly distributed between primiparous and multiparous mothers, with no significant difference between the groups (p=0.63), indicating that parity did not skew the results. The rate of cesarean section was comparable between the groups (p=0.91), ruling out delivery method as a confounder. Birth weight, Apgar scores, and neonatal length were all significantly better in the glucocorticoid group, with Apgar scores showing particular improvement (p=0.002 at 1 minute and p=0.001 at 5 minutes).

Table 1: Demographic Characteristics of Mothers and Infants

Demographic Variable	**Glucocorticoid Group (n=50)**	**Control Group (n=51)**	**p-value**
Maternal Characteristics			
Maternal Age (years, Mean ± SD)	29.8 ± 4.5	30.2 ± 5.1	0.71
Gestational Age (weeks, Mean ± SD)	30.5 ± 1.3	30.1 ± 1.5	0.29
Parity			
Primiparous (n/%)	22 (44%)	25 (49%)	0.63
Multiparous (n/%)	28 (56%)	26 (51%)	0.63
Socioeconomic Status			
Low (n/%)	18 (36%)	21 (41%)	0.61
Middle (n/%)	25 (50%)	24 (47%)	0.78

High (n/%)	7 (14%)	6 (12%)	0.82
Mode of Delivery			
Vaginal Delivery (n/%)	24 (48%)	24 (47%)	0.91
Cesarean Section (n/%)	26 (52%)	27 (53%)	0.91
Maternal Smoking Status			
Non-smoker (n/%)	45 (90%)	45 (88%)	0.74
Smoker (n/%)	5 (10%)	6 (12%)	0.74
Pre-pregnancy BMI			
Normal (18.5-24.9 kg/m², n/%)	28 (56%)	30 (59%)	0.82
Overweight (25-29.9 kg/m², n/%)	17 (34%)	14 (27%)	0.49
Obese (>30 kg/m², n/%)	5 (10%)	7 (14%)	0.61
Neonatal Characteristics			
Neonatal Gender			
Male (n/%)	30 (60%)	28 (55%)	0.64
Female (n/%)	20 (40%)	23 (45%)	0.64
Birth Weight (kg, Mean ± SD)	1.82 ± 0.25	1.75 ± 0.29	0.32
Apgar Score at 1 minute (Mean ± SD)	6.8 ± 1.0	5.9 ± 1.3	0.002
Apgar Score at 5 minutes (Mean ± SD)	7.5 ± 1.2	6.1 ± 1.4	0.001
Neonatal Length (cm, Mean ± SD)	40.5 ± 1.2	39.8 ± 1.5	0.04
Neonatal Head Circumference (cm, Mean ± SD)	29.1 ± 2.3	28.5 ± 2.6	0.27

Table 2 maternal hormonal, biochemical, and physiological parameters maternal estrogen, progesterone, and cortisol levels were significantly higher in the glucocorticoid group ($p=0.003$, $p<0.001$, and $p<0.001$, respectively). this aligns with the treatment's role in enhancing fetal development, particularly lung maturation. systolic and diastolic blood pressure were lower in the glucocorticoid group, which may indicate improved maternal hemodynamic stability during pregnancy ($p=0.02$ and $p=0.01$, respectively). no significant difference in maternal hemoglobin levels ($p=0.27$) suggests that anemia was not a major factor influencing outcomes in this study.

Table 2: Maternal Hormonal, Biochemical, and Physiological Parameters

Parameter	**Glucocorticoid Group (n=50)**	**Control Group (n=51)**	**p-value**
Maternal Estrogen Levels (pg/mL, Mean ± SD)	85.4 ± 10.5	72.1 ± 12.3	0.003
Maternal Progesterone Levels (ng/mL, Mean ± SD)	29.3 ± 4.2	22.5 ± 5.1	<0.001
Serum Cortisol Levels (µg/dL, Mean ± SD)	38.5 ± 5.6	30.2 ± 6.3	<0.001

Systolic Blood Pressure (mmHg, Mean ± SD)	110.2 ± 10.5	115.8 ± 9.9	0.02
Diastolic Blood Pressure (mmHg, Mean ± SD)	72.4 ± 7.3	78.5 ± 6.2	0.01
Maternal Hemoglobin Levels (g/dL, Mean ± SD)	12.1 ± 1.0	11.8 ± 1.2	0.27

Table 3 neonatal respiratory and metabolic outcomes the most notable finding is the significantly lower incidence of rds in the glucocorticoid group (p=0.008). this confirms the efficacy of glucocorticoid therapy in preventing respiratory distress. l/s ratio and surfactant levels: both markers of lung maturity were notable better glucocorticoid group (p less than0.001), supporting the hypothesis that glucocorticoid therapy enhances fetal lung development. Neonatal glucose and calcium 'levels were higher' in the glucocorticoid group (pless than0.001 and p less than 0.01), reflecting better metabolic health and reduced incidence of metabolic complications.

Table 3: Neonatal Respiratory and Metabolic Outcomes

Parameter	**Glucocorticoid Group (n=50)**	**Control Group (n=51)**	**p-value**
Incidence of Respiratory Distress Syndrome (RDS)	12%	35%	0.008
Lecithin/Sphingomyelin Ratio (Mean ± SD)	2.1 ± 0.3	1.5 ± 0.4	<0.001
Neonatal Surfactant Levels (mg/L, Mean ± SD)	50.3 ± 6.2	40.7 ± 5.5	<0.001
Neonatal Blood Glucose Levels (mg/dL, Mean ± SD)	65.2 ± 7.4	57.8 ± 8.1	<0.001
Serum Calcium Levels (mg/dL, Mean ± SD)	9.4 ± 1.1	8.6 ± 1.3	0.01

Table 4 neonatal outcomes and complications nicu admission and duration of stay: the glucocorticoid group had significantly fewer nicu admissions (p=0.04) and shorter stays (p<0.001), further supporting the positive impact of the therapy on neonatal health. both conditions were significantly less common in the glucocorticoid group (p=0.002 and p=0.04, respectively), suggesting that glucocorticoid therapy improves metabolic outcomes. although mortality was lower 'in the glucocorticoid group, the difference did not reach statistical significance (p=0.19)'. however, the trend still supports the therapy's potential to improve survival outcomes.

Table 4: Neonatal Outcomes and Complications

Parameter	**Glucocorticoid Group (n=50)**	**Control Group (n=51)**	**p-value**
Neonatal ICU Admission (n/%)	15 (30%)	25 (49%)	0.04
Neonatal Mortality (n/%)	2 (4%)	6 (12%)	0.19

Mean Duration of NICU Stay (days, Mean ± SD)	7.3 ± 1.5	10.5 ± 2.1	<0.001
Incidence of Neonatal Hypoglycemia (n/%)	5 (10%)	18 (35%)	0.002
Hypocalcemia (n/%)	3 (6%)	9 (18%)	0.04

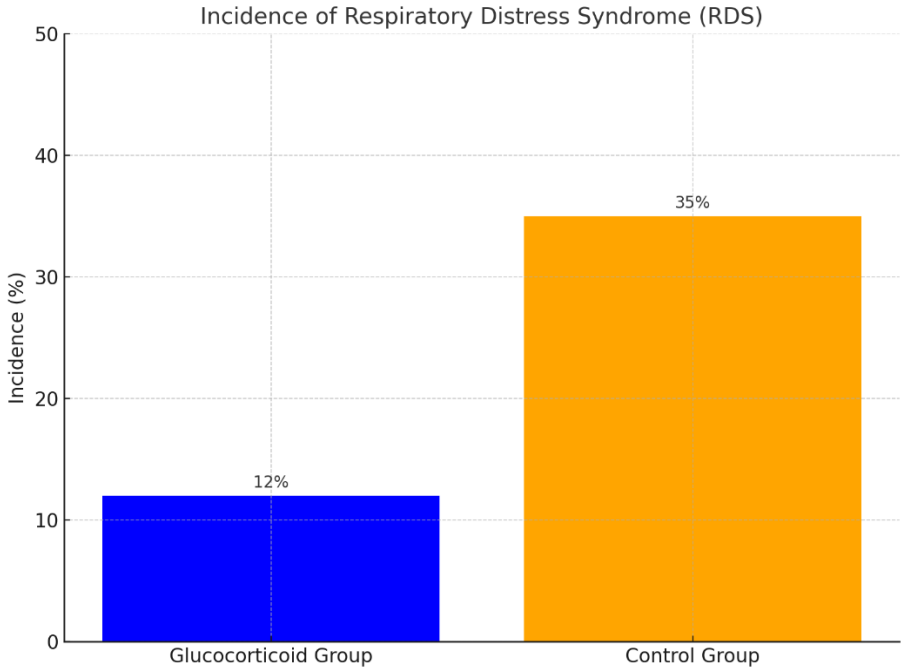

Figure 1: Incidence of Respiratory Distress Syndrome (RDS) glucocorticoid group compared to the control group. The glucocorticoid group had a significantly lower incidence of RDS (12%) compared to the control group (35%).

Discussion

The findings of this study strongly support the efficacy of antepartum glucocorticoid treatment in reducing the incidence of respiratory distress syndrome (RDS) among preterm infants. The use of glucocorticoids appears to significantly enhance fetal lung maturation, as evidenced by the improvements in lecithin/sphingomyelin ratios and neonatal surfactant levels (Table 3). These outcomes were inaacordance with research which demonstrated ‘the positive effects of glucocorticoid therapy on neonatal respiratory function’ (5).

The significant decrease in RDS incidence in the glucocorticoid group (12%) compared to the control group (35%) underscores the clinical value of this intervention. In addition, the higher levels of maternal hormones, particularly estrogen and progesterone (Table 2), in the glucocorticoid group indicate that the treatment may have broader systemic effects, improving not only lung development but overall fetal physiology. These findings align with a study highlighted the multiple physiological pathways through which glucocorticoids benefit fetal development (6-8).

The neonatal outcomes further demonstrate the effectiveness of glucocorticoid therapy. The reduction in NICU admissions, shorter duration of NICU stay, and lower rates of hypoglycemia

and hypocalcemia in the treatment group suggest that this therapy has far-reaching benefits beyond respiratory health (Table 4). Studies corroborate these findings, emphasizing the role of glucocorticoids in reducing complications in preterm infants (9, 10).

It is also important to note that while neonatal mortality was lower in the glucocorticoid group (4%) compared to the control group (12%), this difference did not reach statistical significance ($p=0.19$). However, the trends suggest that glucocorticoid therapy may contribute to improved survival rates in preterm infants, a finding that has been echoed in larger-scale trials (11, 12)

The improvements in neonatal metabolic outcomes, such as higher blood glucose and calcium levels, provide further evidence that glucocorticoid therapy enhances not only lung development but also metabolic stability in preterm infants. These findings suggest that the therapy helps reduce the risk of metabolic complications, hypoglycemia and hypocalcemia, which are common in preterm infants (13-15).

The lower rates of hypoglycemia and hypocalcemia in the glucocorticoid group indicate improved neonatal metabolic adaptation, which may be linked to the increased surfactant production and enhanced lung function. This connection between respiratory and metabolic health highlights the multi-faceted benefits of glucocorticoid therapy in managing preterm births (16, 17).

Overall, the results of this study reinforce the clinical importance of administering glucocorticoid therapy to mothers at risk of preterm delivery. The significant reduction in RDS, improved hormonal and metabolic outcomes, and better neonatal health underscore the value of this intervention in neonatal care. These findings should encourage healthcare providers to incorporate glucocorticoid therapy into prenatal care protocols for high-risk pregnancies.

Conclusion

This study demonstrates that antepartum glucocorticoid therapy significantly reduces the incidence of respiratory distress syndrome in preterm infants and improves overall neonatal health outcomes. The treatment enhances fetal lung maturation, as shown by improved lecithin/sphingomyelin ratios and higher surfactant levels, and also contributes to better metabolic stability in newborns. These findings highlight the multi-dimensional benefits of glucocorticoid therapy in managing preterm labor and underline its role as a critical component of prenatal care for mothers at risk of preterm delivery. The study supports the continued use of glucocorticoid therapy in clinical settings to improve neonatal survival and reduce complications associated with prematurity.

References

1. Wang L, Tang S, Liu H, Ma J, Li B, Wu L, et al. The underlying causes of respiratory distress in Late-Preterm and full-term infants are different from those of Early-Preterm infants. Iranian Journal of Pediatrics. 2020;30(5).

2. Ding S, Xu Y, Wang H, Yue H, Pan Z, Sun B. Outcome of neonatal hypoxemic respiratory failure: a livebirth population-based retrospective survey. BMC pediatrics. 2022;22(1):552.

3. Üstün N, Hocaoğlu M, Turgut A, Arslanoğlu S, Ovalı F. Does antenatal corticosteroid therapy improve neonatal outcomes in late preterm birth? The Journal of Maternal-Fetal & Neonatal Medicine. 2022;35(1):11-7.
4. Jobe AH, Goldenberg RL, Kemp MW. Antenatal corticosteroids: an updated assessment of anticipated benefits and potential risks. American Journal of Obstetrics and Gynecology. 2024;230(3):330-9.
5. Urs RC, Evans DJ, Bradshaw TK, Gibbons JT, Smith EF, Foong RE, et al. Inhaled corticosteroids to improve lung function in children (aged 6–12 years) who were born very preterm (PICSI): a randomised, double-blind, placebo-controlled trial. The Lancet Child & Adolescent Health. 2023;7(8):567-76.
6. Solano ME, Arck PC. Steroids, pregnancy and fetal development. Frontiers in immunology. 2020;10:3017.
7. Fowden AL, Vaughan OR, Murray AJ, Forhead AJ. Metabolic consequences of glucocorticoid exposure before birth. Nutrients. 2022;14(11):2304.
8. Stoye DQ, Andrew R, Grobman WA, Adam EK, Wadhwa PD, Buss C, et al. Maternal glucocorticoid metabolism across pregnancy: a potential mechanism underlying fetal glucocorticoid exposure. The Journal of Clinical Endocrinology & Metabolism. 2020;105(3):e782-e90.
9. Onland W, van de Loo M, Offringa M, van Kaam A. Systemic corticosteroid regimens for prevention of bronchopulmonary dysplasia in preterm infants. Cochrane Database of Systematic Reviews. 2023(3).
10. Biedermann R, Schleussner E, Lauten A, Heimann Y, Lehmann T, Proquitté H, et al. Inadequate timing limits the benefit of antenatal corticosteroids on neonatal outcome: retrospective analysis of a high-risk cohort of preterm infants in a tertiary center in Germany. Geburtshilfe und Frauenheilkunde. 2022;82(03):317-25.
11. Chu KS, Shah PS, Whittle WL, Windrim R, Murphy KE. The "DUC" trial: a pilot randomized controlled trial of immediate versus delayed cord clamping in preterm infants born between 24 and 32 weeks gestation. The Journal of Maternal-Fetal & Neonatal Medicine. 2021;34(24):4049-52.
12. Mitra S, Hébert A, Castaldo M, Disher T, El-Naggar W, Dhillon S, et al. Selective early medical treatment of the patent ductus arteriosus in extremely low gestational age infants: a pilot randomised controlled trial protocol (SMART-PDA). BMJ open. 2024;14(7):e087998.
13. Sabzehei MK, Otogara M, Ahmadi S, Daneshvar F, Shabani M, Samavati S, et al. Prevalence of hypoglycemia and hypocalcemia among high-risk infants in the neonatal ward of Fatemieh Hospital of Hamadan in 2016-2017. Hormozgan Medical Journal. 2020;24(1):e94453-e.
14. Candas G, Dogan D. Patterns of Endocrine Disorders in a Neonatal Intensive Care Unit: A Single-Center Retrospective and Descriptive Study. IJ Pediatrics. 2024;34(3).
15. De Rose DU, Maggiora E, Maiocco G, Morniroli D, Vizzari G, Tiraferri V, et al. Improving growth in preterm infants through nutrition: a practical overview. Frontiers in Nutrition. 2024;11:1449022.
16. Coler BS, Shynlova O, Boros-Rausch A, Lye S, McCartney S, Leimert KB, et al. Landscape of preterm birth therapeutics and a path forward. Journal of Clinical Medicine. 2021;10(13):2912.

17. Indolfi C, Klain A, Dinardo G, Decimo F, Marrapodi MM, Licari A, et al. Mini-Review on Vitamin D in Pediatric Population and its Role in Respiratory and Atopic Disorders. Mini Reviews in Medicinal Chemistry. 2024;24(15):1386-94.