EVALUATE THE IMPORTANCE OF GIVING ANTENATAL CORTICOSTEROIDS IN RESPIRATORY DISTRESS SYNDROME IN PRETERM NEONATES

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Abstract

Respiratory distress syndrome (RDS) is one of the leading causes of early neonatal morbidity and mortality in late preterm infants (LPIs) worldwide.

The aim: The study is intended to evaluate the importance of giving antenatal corticosteroids in decreasing respiratory distress syndrome in preterm neonates.

Materials and methods: Prospective cohort study done in all preterms delivered in the hospital attached to those admitted in our neonatal intensive care unit during the study duration are taken as the source. All preterm babies are admitted to the neonatal intensive care unit.

Results: The overall incidence of RDS in this study was 30 (15 %), among which 7 (7 %) were exposed to steroids, and 23 (23 %) were not exposed to steroids. Antenatal corticosteroids were significantly associated with reduced incidence of RDS in preterms (neonates born between 28–37 weeks of gestational age). The overall incidence of TTN *(*transient tachypnea*)* was found to be 46 (28 %) in this study, among which 14 (14 %) were exposed to steroids, and 32 (32 %) were not exposed to steroids. Antenatal corticosteroids were significantly associated with reduced incidence of TTN in preterms. Antenatal corticosteroids significantly reduce the need for supplemental oxygen, NICU admission, need for CPAP and mortality rate. The dose of antenatal corticosteroids was significantly associated with the incidence of RDS and TTN. 2 doses of steroids reduced RDS and TTN significantly compared to the single dose, which was just significantly associated. This study found no significance between RDS and TTN with gestational age, mode of delivery, birth weight and RDS among steroid-exposed babies.

Conclusion: The use of antenatal corticosteroids should be promoted because they successfully lowered morbidity and mortality among premature newborns in the population studied. In order to optimise proper and timely prenatal corticosteroid treatment, this study underlines the necessity for quality improvement initiatives.

Keywords: gestational age, premature newborns, antenatal corticosteroids, respiratory distress syndrome, transient tachypnea, birth weight, morbidity, mortality, continuous positive airway pressure, and mechanical ventilation.

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1. Introduction

Respiratory distress syndrome is the most common complication observed in preterm neonates. An established intervention is administering corticosteroids to pregnant women at risk of preterm

birth to reduce the severity of neonatal respiratory distress syndrome. Studies showed a significant reduction in the incidence of respiratory distress syndrome in preterm babies whose mothers had received antenatal corticosteroids. Respiratory disorders vary from 29.9 to 54 % in India. The major causes of RDS comprise pneumonia, aspiration syndrome, transient tachypnea and hyaline membrane disease (HMD). The frequency of HMD among cases of respiratory disorders varies from 0 to 9.2 in India, as against 42.2 to 60 % of the cases in the West. In view of the variability of the data from various parts of India [1].

Corticosteroid production is thought to improve surfactant production, and there is also an associated reduction in the risk of neonatal intraventricular haemorrhage, necrotising enterocolitis, hyperbilirubinaemia, and neonatal death. What remains unclear, however, is whether repeat doses should be given if delivery does not occur shortly after the initial course. The antenatal administration of corticosteroids to pregnant women at risk of preterm delivery between 24 and 34 weeks of gestation is recommended to accelerate lung maturation and reduce the incidence of RDS, among other beneficial effects. Infants born preterm between 35 and 36 weeks gestation have a higher incidence of respiratory complications than infants born preterm due to immaturity, with a reduced catecholamine response and an increase in lung fluid retention.

One of the most vital roles of glucocorticoids in normal fetal development is their effects on pulmonary maturation, lowering the risk of respiratory distress in preterm infants. Glucocorticoids also play a vital role in fetal brain development by initiating terminal neuronal maturation, remodelling axons and dendrites, and affecting cell survival. Besides its effects on the fetal lungs and brain, GC has important effects on other organ systems such as the heart, circulation, kidneys, liver, adipose and thyroid, all contributing to improving postnatal adaptation. Glucocorticoids also affect systems that regulate fetal growth and profoundly influence the development and lifelong function of the HPA axis.

RDS is one of the most serious complications of preterm birth and the primary cause of early neonatal death. It affects up to 80–90 % of extremely preterm infants and about half of the very preterm infants, but it can also affect infants born at later gestations. RDS usually presents at birth or shortly thereafter. The progressive symptoms include grunting, chest wall retractions, nasal flaring, and increased work breathing. In the infant's lung, the surfactant is produced by type II pneumocytes in the alveolar airspaces. Surfactant forms a film in the alveoli, lowering alveolar surface tension, thus increasing lung compliance and preventing atelectasis. The pathophysiology behind the disease can briefly be explained by the structurally immature and surfactant-deficient lung that has a tendency to collapse. The presence of relatively well-perfused but poorly ventilated areas of the lung results in ventilation/perfusion mismatch with hypoxemia and hypercarbia. If left untreated, the condition may lead to respiratory failure and death. The treatments for RDS include surfactant replacement therapy, continuous positive airway pressure (CPAP), and mechanical ventilation [2].

Corticosteroids interact with specific receptor proteins in the target tissues as they regulate the expression of the genes responsive to corticosteroids. Hence, the deposition of the proteins synthesised by the various target tissues is altered. In this way, corticosteroids assist in achieving a successful transition from fetal to extrauterine life, accelerating fetal maturation. The acceleration of lung development reduces the incidence of respiratory distress syndrome and its severity; in view of this, antenatal corticosteroids prove to be beneficial to preterm babies in reducing respiratory distress syndrome [3]. Hence we study the role of antenatal corticosteroids in decreasing respiratory distress syndromes in preterm neonates.

The aim of the research: The study intends to evaluate the importance of antenatal corticosteroids in decreasing respiratory distress syndrome in preterm neonates.

2. Materials and methods

A prospective cohort study done in all preterms delivered in the hospital attached to SVS Medical College, Mahabubnagar and those admitted in our neonatal intensive care unit during the study duration is taken as the source. All preterm babies are admitted to the neonatal intensive care unit.

Duration of study: 2 years of study from September 2019 to September 2021.

Sample size:

The sample size was calculated using the following formula: $N = \frac{Z^2 \cdot P \cdot (1-P)}{D2}$

Where N = the expected minimum sample.

Z = the standard value, which corresponds to 1.96 at a 95 % confidence interval

P = Estimated prevalence (29 %) in *Wang ML* et al. study.

D = Margin of error taken as 6 %

Sample size is = $\frac{1.96 \cdot X \cdot 1.96 \cdot X29 \cdot X71}{36} = 219$

The sample size was calculated with open-source software, with an assumed 29 % rate of respiratory disorders in preterm infants, an α error of 5 %, and 80 % power to detect a reduction of 50 % in the rate of respiratory disorders with corticosteroids. This resulted in a required sample size of 219 (100 in each group).

Inclusion criteria: All babies born to mothers with gestational age <37 weeks who received antenatal corticosteroids as cases.

Exclusion criteria: All mothers who received steroids for any other medical illness. Neonates with major congenital malformations.

Bioethics approval of SVS Medical College, the number is SVSM/Pg/2019-022, dated-14-12-2019.

A detailed history was taken, including maternal history, LMP, gestational age, medical history, date, time and the number of doses of corticosteroids taken by the mother antenatally. Gestational age was defined according to the date of the woman's last menstrual period, if known and reliable, or by ultrasonography before 20 weeks of pregnancy.

Details of the examination of the baby, including Ballard score, systemic examination, respiratory distress score, APGAR score, chest X-ray, the need for surfactant, and the need for intubation, are noted.

All preterm babies whose mother has received antenatal steroid are taken as cases, and those not receiving antenatal steroids are taken as controls.

Cases: 100 women receive betamethasone.

Controls: 100 women received a placebo.

Each ampoule of betamethasone contained 6 mg (3 mg acetate and 3.9 mg disodium phosphate). The placebo ampoules contained a similar volume of 0.9 % saline solution. The study took no part in the women's prepartum or postpartum management or neonatal management. Women in premature labour underwent tocolysis, per the routine hospital practice, to postpone delivery and allow the full course of medication to be administered. The neonatologist who followed up on the infants prospectively collected data on the pregnant women and their newborns on a standardised form.

If the woman delivered before she received the second dose of the medication, she was analysed as part of the group. All Basic investigations, including ABG and chest X-ray, were done in all cases and controls.

Outcomes evaluated

The primary outcomes were the occurrence of neonatal respiratory disorders: respiratory distress syndrome or transient tachypnoea of the newborn, defined by the presence of respiratory distress for more than two hours after birth and characterised by tachypnoea, expiratory grunting, chest wall retractions, flaring of the nostrils, cyanosis, and a growing need for oxygen. We used radiological criteria to differentiate between the two disorders used: diffuse reticulogranular infiltrate in respiratory distress syndrome and thickening of the bronchovascular bundle, pulmonary hypermutation, and the presence of fluid in the interlobar fissures in transient tachypnoea of the newborn.

The secondary outcomes included type of delivery and neonatal outcomes: gestational age at birth, birth weight, Apgar scores at one and five minutes; treatment with an exogenous surfactant, ventilatory support, and admission to intensive care; neonatal hypoglycaemia, neonatal jaundice, the persistence of ductus arteriosus, neonatal sepsis, and neonatal morbidity and duration of stay in hospital and death.

Statistical analysis

Statistical analysis was performed with SPSS software. The baseline characteristics of the participants in each group were compared with Student's *t*-test for continuous variables with normal distribution and the Mann-Whitney U test for discrete and ordinal variables or those with non-normal distribution. Categorical variables were compared with Pearson's χ^2 test or Fisher's exact test, as appropriate. P values for all tests were two-tailed, and the significance level was defined at 5 %. The same tests were used to determine the effects of corticosteroid treatment on perinatal outcomes. The number needed to treat was calculated with its 95 % confidence interval for the outcomes in which we found a beneficial effect of corticosteroid treatment.

3. Results

There is no significance in age groups, gravida, gestation in weeks, and mode of delivery in both groups if the p-value is >0.05 (**Table 1**).

Table 1

Demographic-wise distribution of mother

Age of mother in years	Controls	Cases	Total
18–24	47 (47 %)	49 (49 %)	96 (48 %)
25–29	31 (31 %)	27 (27 %)	58 (29 %)
30–35	18 (18 %)	19 (19 %)	37 (16.5 %)
>36	4 (4 %)	5 (5 %)	9 (4.5 %)
Mean±SD	25.3±4.2	27.1±3.8	26.2±4.0
Total	100	100	200
Gravida			
Primigravida	51 (51 %)	55 (55 %)	106 (53 %)
Multigravida	49 (49 %)	45 (45 %)	94 (47 %)
Mean±SD	50±1.41	50±7.0	100±8.4
Gestational age in weeks			
less than 28 weeks	9 (9 %)	10 (10 %)	19 (9.5 %)
28 to 32 weeks	26 (26 %)	27 (27 %)	53 (26.5 %)
32 to 37 weeks	65 (65 %)	63 (63 %)	128 (64 %)
Mean±SD	26.23±5.1	30±3.5	28±4.6
Mode of Delivery			
NVD	55 (55 %)	53 (53 %)	108 (54 %)
LSCS	45 (45 %)	47 (47 %)	92 (46 %)
Mean±SD	50±7.0	50±4.2	100±11.3

Premature labour is the main cause of antenatal corticosteroids induced in patients (**Table 2**).

Table 2

Associated condition in mother

Associated condition	Controls	Cases	Total
Hypertension	24 (24 %)	27 (27 %)	51 (25.5 %)
Premature rupture of membranes	39 (39 %)	43 (43 %)	82 (41 %)
Premature labour	64 (64 %)	66 (66 %)	130 (65 %)
Diabetes	3 (3 %)	2 (2 %)	5 (2.5 %)
Fetal growth restriction	1 (1 %)	1 (1 %)	2 (1 %)
Oligohydramnios	4 (4 %)	3 (3 %)	7 (3.5 %)
Others	8 (8 %)	9 (9 %)	17 (8.5 %)
Received tocolytics	62 (62 %)	63 (63 %)	125 (62.5 %)

Among the 100 cases, most of them, i.e., 77 (77 %), received two doses between 1–7 days before birth (**Fig. 1**).

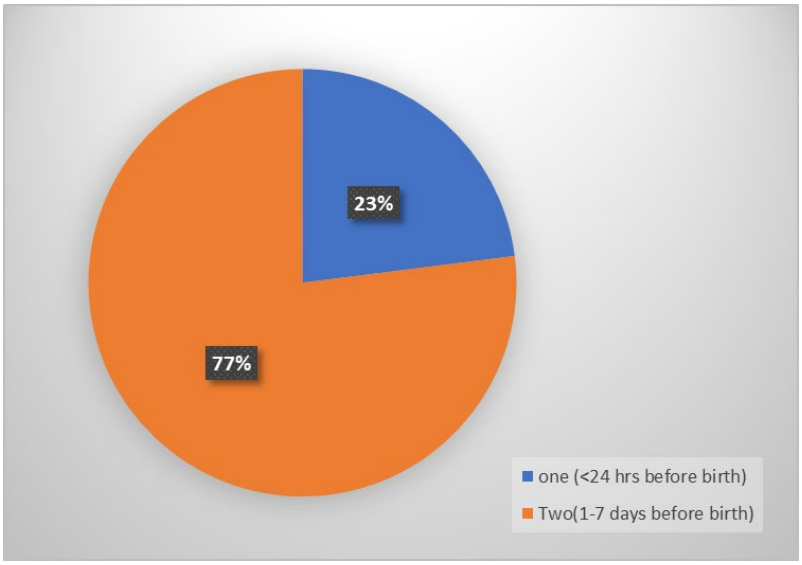

Fig. 1. Pie diagram showing the number of doses of steroids

Among the control, 59 % were male, and 41 % were females. Among cases, 58 % were male, and 42 % were female. There is no significance between cases and controls.

In < 2 kgs, babies were 30 % in controls and 29 % in cases; in 2–2.5 kgs, babies were 61 % in controls and 58 % in cases and in >2.5 kgs, babies were 9 % in controls and 13 % in cases (**Table 3**).

Table 3

Newborn baby gender and weight-wise distribution

Sex	Controls	Cases	Total
Male	59 (59 %)	58 (58 %)	117 (56.5 %)
Female	41 (41 %)	42 (42 %)	83 (41.5 %)
Mean±SD	50±12.72	50±11.3	100±24.0
Birth Weight			
<2 kgs	30 (30 %)	29 (29 %)	59 (29.5 %)
2–2.5 kgs	61 (61 %)	58 (58 %)	119 (58.5 %)
>2.5 kgs	9 (9 %)	13 (13 %)	22 (11 %)
Mean±SD	33.3±26.1	33±22.8	66±48.9

The overall incidence of RDS in this study was 30 (15 %), among which 23 were from controls, and 7 were among cases, and the values were statistically very significant (p = 0.0001). The overall incidence of TTN was 46 (28 %) in this study, among which 32 were from controls and 14 among cases, and the values were statistically very significant (p = 0.0001) (**Table 4**).

Table 4

Incidence of RDS and TTN

RDS/TTN	Controls	Cases	Total	P-Value
RDS	23 (23 %)	7 (7 %)	30 (15 %)	<0.00001*
TTN	32 (32 %)	14 (14 %)	46 (28 %)	<0.00001*
Total	55 (55 %)	21 (7 %)	76 (38 %)	

*Note: *p-value is significant statistically; RDS – respiratory distress syndrome; TTN – transient tachypnea of the newborn*

APGAR score at one minute is 24 % in controls and 16 % in cases, whereas, at 5 minutes, it is 21 % in controls and 9 % in cases which is significant at 1 and 5 minutes APGAR scores (**Table 5**).

Table 5
APGAR score of Babies at Birth in Two groups studied

	Controls	Cases	Total	P-Value
		At 1 min		
<7	24 (24 %)	16 (16 %)	40 (20 %)	<0.001
>7	76 (76 %)	78 (78 %)	160 (80 %)	<0.001
		At 5 min		
<7	21 (21 %)	9 (9 %)	30 (15 %)	<0.001
>7	79 (38.5 %)	87 (43.5 %)	170 (85 %)	<0.001

*Note: *p-value is significant statistically*

65 % received routine care at birth; values were very strongly significant statistically (p = 0.0001); 30.5 % required supplemental oxygen; values were very strongly significant statistically (p = <0.0001); 4.5 % of babies required intubation and positive pressure ventilation; values were not significant statistically (p = 0.47).

Of the 62 babies admitted to the neonatal intensive care unit, the two groups had no statistical significance. (p = 0.56), 16.5 % of babies required supplemental oxygen; values were significant statistically. (p = 0.0004), values were significant statistically (p = 0.0001). Among them, 6 were from controls, and 1 was from cases, and the values were not statistically significant (p = 0.1531) (**Table 6**).

Table 6
Resuscitation at birth in two groups studied

Resuscitation at Birth	Controls	Cases	Total	P-Value
Routine care	48 (48 %)	82 (82 %)	130 (65 %)	<0.001
Supplemental O_2	47 (47 %)	14 (14 %)	61 (30.5 %)	<0.001
Intubated	5 (5 %)	4 (4 %)	9 (4.5 %)	0.4716
		COURSE IN NICU		
Under observation	5 (5 %)	2 (2 %)	7 (3.5 %)	0.1499
Under Oxygen	26 (26 %)	7 (7 %)	33 (16.5 %)	0.0004*
CPAP	12 (12 %)	3 (3 %)	15 (7.5 %)	0.0001*
Ventillator	6 (6 %)	1 (1 %)	7 (3.5 %)	0.5617

*Note: *p-value is significant statistically*

Of 100 babies receiving steroids, 9 (9 %) had RDS. Of them, 3 belonged to <28 weeks of gestation, 3 from 28–32 weeks, and 3 from 32–37 weeks. The values were not statistically significant (p = 0.9). Of 100 babies receiving steroids, 14 (14 %) had TTN. In them 5 (5 %) belonged to <28 weeks of gestation, 3 (3 %) from 28–32 weeks of gestation and 4 (4 %) from 32–37 weeks of gestation. The values were not statistically significant (p = 0.8) (**Table 7**).

Table 7
Association of RDS, TTN with Gestational Age among Cases

Variables	<28 weeks	28–32 weeks	32–37 weeks	Total	P-value
With RDS	3 (3 %)	3 (3 %)	3 (3 %)	9 (9 %)	0.9
With TTN	5 (5 %)	3 (3 %)	4 (4 %)	12 (12 %)	0.8
Without RDS/TTN	21 (21 %)	23 (23 %)	35 (35 %)	79 (79 %)	0.7

*Note: *p-value is significant statistically*

Out of 100 babies receiving steroids, 7 (7 %) had RDS. Of them, 5 received a single steroid dose, and 2 received 2 doses. The values were significant statistically (p = 0.0239). Of 100 babies receiving steroids, 14 (14 %) had TTN. Of them, 8 received a single steroid dose, and 6 received 2 doses. The values are not statistically significant (p = 0.5). Out of 100 babies, 79 (79 %) dint RDS/TTN. Among them, 20 received a single steroid dose, and 59 received 2 doses. The values were very strongly significant statistically (p = <0.0001) (**Table 8**).

Out of 100 babies receiving steroids, 7 (7 %) had RDS. In them 4 (4 %) were of birth weight <2 kgs, 2 (2 %) of birth weight 2–2.5 kgs and 1 (1 %) was of birth weight >2.5 kgs. The values were not statistically significant (p = 0.8). Out of 100 babies receiving steroids, 14 (14 %) had TTN. In them 6 (6 %) were of birth weight <2 kgs, 5 (5 %) of birth weight 2–2.5 kgs and 3 (3 %) was of birth weight >2.5 kgs. The values were not statistically significant (p = 0.9) (**Table 9**).

Table 8

Association of RDS and TTN with doses of Steroids among cases

Dose of steroid-associated RDS and TTN	One dose	Two doses	Total	P-value
With RDS	5 (5 %)	2 (2 %)	7 (7 %)	0.02
With TTN	8 (8 %)	6 (6 %)	14 (14 %)	0.5
Without RDS/TTN	20 (20 %)	59 (59 %)	79 (79 %)	<0.001*

*Note: *p-value is significant statistically*

Table 9

Association of RDS and TTN with Birth weight among cases

The birth weight associated with RDS and TTN	<2 kgs	2–2.5 kgs	>2.5 kgs	Total	P-value
With RDS	4 (4 %)	2 (2 %)	1 (1 %)	7 (7 %)	0.8
With TTN	6 (6 %)	5 (5 %)	3 (3 %)	14 (14 %)	0.9
Without RDS/TTN	37 (37 %)	21 (21 %)	11 (11 %)	69 (69 %)	0.9

*Note: *p-value is significant statistically*

Rates of jaundice (57 % vs 54 %), hypoglycaemia (17 % vs 7 %), and sepsis (6 % vs 4 %) were similar in the two groups. Nevertheless, the rate of jaundice requiring phototherapy was lower in babies whose mothers had received corticosteroids (34 % vs 23 %); P = 0.01). There was no difference in the outcomes of neonatal morbidity (65 % vs 54 %), admission to intensive care (33 % vs 35 %), or rate of neonatal death (two (2 %) in the placebo group). The deaths in the placebo group were associated with severe perinatal asphyxia (**Table 10**).

Table 10

Complications and neonatal outcomes in infants

Neonatal complications	Controls	Cases	P-value
Jaundice	57 (57 %)	54 (54 %)	0.6
Jaundice requiring phototherapy	34 (34 %)	23 (23 %)	0.001*
Hypoglycaemia	7 (7 %)	11 (11 %)	0.3
Neonatal sepsis	6 (6 %)	4 (4 %)	0.5
Neonatal morbidity	65 (65 %)	54 (54 %)	0.8
Admission to intensive care	33 (33 %)	35 (35 %)	0.8
Neonatal death	4 (4 %)	0	0.09
<4 days in the hospital	40 (40 %)	32 (32 %)	0.7
Mean (SD) days in the hospital	6.1	5.5	0.6

Out of 200 babies in this study, 196 (98 %) improved and were discharged. Among them, 100 % were from cases, and 96 (96 %) were from controls. The value was not significant statisti-

cally (p = 0.08). Of 200 babies, 4 (2 %) died, all 4 from controls. The value was very significant statistically (p = 0.04) (**Fig. 2**).

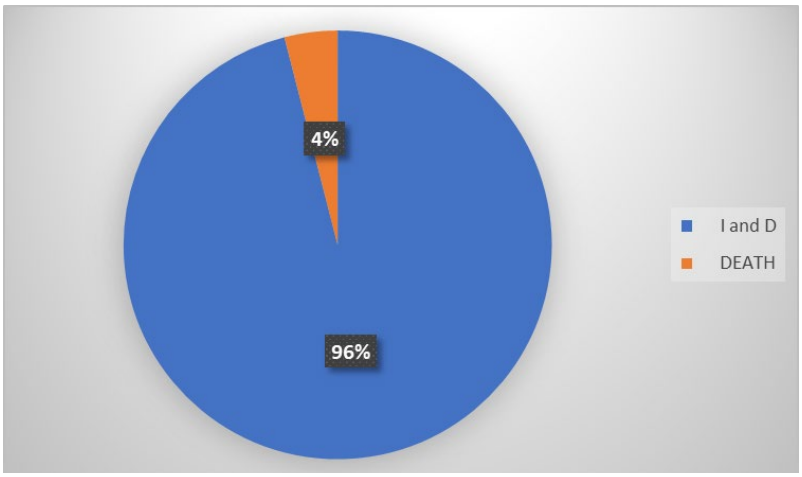

Fig. 2. Pie diagram showing the death rate in the study

4. Discussion

Antenatal administration accelerates the effect of endogenous corticosteroids and induces the production of all the known components of the surfactant system. As respiratory distress syndrome is characterised by a qualitative and quantitative deficiency of pulmonary surfactants, infants born before 34 weeks gestation, in whom the incidence of this syndrome is higher, benefit from the administration of antenatal corticosteroids [3]. Respiratory distress syndrome, however, is much less common in late preterm infants, in whom the principal respiratory disorder is transient tachypnoea. We have done a study to evaluate the importance of antenatal corticosteroids in decreasing respiratory distress syndrome in preterm neonates with a gestational age of less than 37 weeks. Demographic details such as age, gravida, associated conditions, and mode of delivery are comparable in the 2 groups.

The overall incidence of RDS in this study was 15 %, and the values were statistically very significant when compared in controls than cases (23 % vs 7 %) (p = 0.0001). The overall incidence of TTN was found to be 28 % in this study, and values were statistically very significant compared to controls than cases (32 % vs 14 %) (p = 0.0001). In a study by Porto and colleagues in 2011, they found the rate of RDS was low (2 (1.4 %) in the corticosteroid group; 1 (0.8 %) in the placebo group; P = 0.54), while the rate of transient tachypnoea was high in both groups (34 (24 %) vs 29 (22 %). In a Gyamfi-Bannerman C et al. study, respiratory distress syndrome was 7.5 % in corticosteroids exposed babies delivered between 34–36 weeks. In the Yadav et al. study of steroids at 24–28 weeks, although there was no difference in the incidence of respiratory distress syndrome (RDS), it was less severe. Htun ZT et al. study recommends that maternal antenatal corticosteroids are recommended for possible preterm delivery in the next seven days between the 23rd and 34th week gestational age. Some institutions offer antenatal corticosteroids at 22 weeks if anticipating delivery within the next week. Despite multiple interventions targeting various etiologies, the goal of preventing preterm birth remains elusive.

In the present study, the APGAR score at one minute is 24 % in controls and 16 % in cases, whereas, at 5 minutes, it is 21 % in controls and 9 % in cases which is significant at 1 and 5 minutes APGAR scores. Rodriguez A et al. [8] study the comparison of the Apgar score at the first and fifth minutes between the patients who received antenatal corticosteroids and those who did not; the newborns exposed to corticosteroid therapy presented a significantly greater average Apgar score at the first minute of life than those who were not. The higher Apgar scores for patients who received antenatal corticosteroids probably reflect the role that this class of medication plays in the cardiovascular and respiratory stabilisation of premature neonates. A study done by Ana Maria Feitosa Porto et al. [9] showed no significance at 1 and 5 minutes of APGAR scores.

In previous studies, it is less when compared with our study. The differences could be due to individual observer variation, given the subjective nature of the Apgar scoring system. In most previous studies, the scoring system was made by experienced persons, but only a few had individuals whose primary responsibility was that of observing and scoring the newborn. Corticosteroids are also thought to promote an increase in the expression of adrenergic receptors in vessel walls and the myocardium, which assist in cardiocirculatory stabilisation at birth. This being so, the higher average Apgar score at the first minute for patients exposed to antenatal corticosteroid therapy, observed in this study, may represent a greater capacity among premature infants for adaptation to the extrauterine environment.

In the present study, 65 % received routine care at birth, and the values were very strongly significant statistically (p = 0.0001); 30.5 % required supplemental oxygen, and the values were very strongly significant statistically (p = <0.0001), 4.5 % of babies required intubation and positive pressure ventilation, and the values were not statistically significant. (p = 0.47). In a study by Wagh S Amargeetet al [10], 14 % of late preterm babies (n = 114) required some resuscitation. The need for resuscitation – Initial steps of resuscitation (4.3 % vs 0.4 %), Positive pressure ventilation at birth (9.7 % vs 1.3 %) and intubation (0.8 % vs 0.001 %) were higher in preterm. None of the babies in the study period required chest compressions or medications for resuscitation. The need for resuscitation was higher at 34 and 35 weeks as against babies born at 36 weeks (18 % vs 9 %).

Of the 62 babies admitted to the Neonatal intensive care unit, 3.5 % of babies were under observation for respiratory distress. There was no statistical significance between the two groups (p = 0.56), 16.5 % of babies required supplemental oxygen. And the values were significant statistically (p = 0.0004), 7.5 % of babies required CPAP, and the values were significant statistically (p = 0.0001), 3.5 % of babies required mechanical ventilation. Among them, 6 were from controls, 1 was from cases, and the values were not statistically significant (p = 0.1531) in a study by Gyamfi-Bannerman et al., [11] NICU admission among late preterms was higher. Deshmukh M et al. [13] conclude that ANC exposure reduced the need for respiratory support in late preterm neonates.

Ana Maria Feitosa Porto et al. [9] showed in both groups, there were low rates of respiratory distress syndrome (two cases (1.4 %) in the corticosteroid group and one case (0.8 %) in the placebo group; P = 0.54) and high rates of transient tachypnoea of the newborn (34 cases (24 %) vs 29 cases (22 %); P = 0.77). Treatment with corticosteroids failed to reduce the risk of any respiratory morbidity (risk ratio 1.09, 95 % confidence interval 0.72 to 1.66). Only one baby in the corticosteroid group required exogenous surfactant. The necessity for ventilatory support was also similar, at around 20 % in both groups (28 cases (20 %) in the corticosteroid group and 24 cases (19 %) in the placebo group). There was no difference in the type of ventilatory support used, and the mean duration of ventilation was 2.2 days in the infants in the corticosteroid group and 2.8 days in the placebo group (P = 0.65).

Of 100 babies receiving steroids, 9 (9 %) had RDS. Of them, 3 % belonged to <28 weeks of gestation, 3 % from 28–32 weeks of gestation and 3 % from 32–37 weeks of gestation. The values were not statistically significant. (p = 0.9) A study by Natalie M et al. [14] showed the incidence at 36 weeks (53.9 %), followed by those born at 35 weeks (28.4 %) and at 34 weeks (17.8 %), respectively.

A consortium of safe labour documented that the incidence of RDS was 40.1 %, 21.9 % and 9.1 % at 34, 35 and 36 weeks of gestation, respectively. In a study by William et al., it was found that at a gestational age of 34, 35 and 36 weeks, RDS was seen in 30, 14 and 7.1/1000 infants. In the latest revision of Crowley's meta-analysis, [6] the use of antenatal corticosteroids led to a significant reduction in the incidence of respiratory distress syndrome, with the value of the odds ratio (OR 0.53; 95 % CI: 0.44–0.63).

In our study, out of 100 babies receiving steroids, 14 (14 %) had TTN. In them 5 (5 %) belonged to <28 weeks of gestation, 3 (3 %) from 28-32 weeks of gestation and 4 (4 %) from 32–37 weeks of gestation. The values were not statistically significant (p = 0.8). Chavan S et al. found the incidence of TTN was 16 per 1000 live births. A review of unpublished five

years (2010–2016) of data from All India Institutes of Medical Sciences (AIIMS), a public sector apex referral centre in India's capital, reported the incidence of TTN to be as high as 46.6 per 1000 live births [16].

In our study, out of 100 babies, 79 (79 %) dint RDS/TTN. Among them, 20 received a single steroid dose, and 59 received 2 doses. The values were very strongly significant statistically.

In the present study, out of 100 babies receiving steroids, 7 (7 %) had RDS 14 (14 %) had TTN. In RDS 4 (4 %) were of birth weight <2 kgs, 2 (2 %) of birth weight 2–2.5 kgs and 1 (1 %) was of birth weight >2.5 kgs. The values were not statistically significant ($p = 0.8$). In TTN 6 (6 %) were of birth weight <2 kgs, 5 (5 %) of birth weight 2–2.5 kgs and 3 (3 %) was of birth weight >2.5 kgs. The values were not statistically significant. ($p = 0.9$) Antenatal corticosteroid utilisation covers around 70 % of newborns of very low weight at 14 American centres that belong to the NICHD Neonatal Research Network [17]. In Latin America, the few data available indicate that corticosteroids are used on around 30 % of pregnant women with premature deliveries. In Brazil, there are some reports of antenatal corticosteroid use for inducing fetal lung maturation. In a study Kamath-Rayne BD et al. [18], many patients who receive tocolytic treatment for threatened preterm birth do not receive antenatal glucocorticoid treatment as recommended. Recommended treatment based on apparent evidence should be performed for patients with threatened preterm birth.

In the present study, complications in newborns, such as jaundice, hypoglycaemia, and sepsis, were similar in the two groups. Nevertheless, the rate of jaundice requiring phototherapy was lower in babies whose mothers had received corticosteroids (34 % vs 23 %); $P = 0.01$. There was no difference in the outcomes of neonatal morbidity (65 % vs 54 %), admission to intensive care (33% vs 35%), or rate of neonatal death (two (2 %) in the placebo group). The deaths in the placebo group were associated with severe perinatal asphyxia.

Mwita S et al. studied 356 (35.3 %) women who were administered at least one dose of ACS between 24 to 34 weeks gestation and 385 (34.2 %) infants exposed to ACS. Infants exposed to ACS had a lower rate of perinatal mortality (13.77 %) compared to those who were not exposed (28.38 %). Multivariate analysis indicated that infants exposed to ACS were less likely to die during the perinatal period, with a RR of 0.34 (95 %CI 0.26–0.44). Only one-third of the sample was provided with ACS.

In our study, out of 200 babies, 196 (98 %) improved and got discharged. Among them, 100 % were from cases, and 96 (96 %) were from controls. The value was not statistically significant ($p = 0.08$).

Of 200 babies, 4 (2 %) died, all 4 from controls. The value was very significant statistically ($p = 0.04$). In a study by Escobar G J et al., [14] the mortality rate among late preterms was 0.8 %. In a study by Robert D et al. [7], combined fetal and neonatal death was significantly reduced in corticosteroid-treated infants at a gestation of at least 34 weeks (RR 1.13, 95 % CI 0.66 to 1.96, 770 infants) before 36 weeks (RR 0.75, 95 % CI 0.61 to 0.94, 969 infants) but at 36 weeks, there was a non-significant trend towards an increase in combined fetal and neonatal death (RR 3.25, 95 % CI 0.99 to 10.66, 498 infants).

In the present study, the fact that the magnitude of the protective role of antenatal steroids is close to that found during the period before exogenous surfactants were available in developed countries reflects the neonatal pattern in respiratory affections is still an important cause of death among newborns [1]. However, when the use of the medication was analysed together with other factors that could interfere with neonatal mortality, antenatal corticosteroids persisted as a protective factor in the cohort studied. It is known that antenatal corticosteroids increase the survival of neonates that previously would not have had the chance of survival. Consequently, such patients come to present complications resulting from the prolonged hospital stay, such as neonatal sepsis, necrotising enterocolitis and chronic lung disease, among others. Such complications, in their turn, may contribute to neonatal mortality. This being so, when all these factors are analysed together, the protective role of corticosteroids in the survival of premature infants is evident.

However, suppose antenatal corticosteroids have a beneficial effect at very early gestational ages. In that case, it may be more evident in mortality rates and neurological morbidity than

in the prevention of RDS. Evidence from the EPICure study, a prospective cohort study of all infants born at less than 26 weeks gestation in the United Kingdom and Ireland, showed that exposed newborns had decreased rates of death (OR 0.57, 95 % CI 0.37–0.85) and severe IVH (OR 0.39, 95 % CI 0.22–0.77), but not a decreased rate of RDS. A more recent retrospective cohort study of 181 infants born at 23 weeks gestation also showed that antenatal corticosteroids decreased the risk of death (OR 0.32, 95 % CI 0.12–0.84) relative to unexposed infants. A retrospective series from Japan even demonstrated a decrease in mortality of infants born at 22 or 23 weeks gestation after exposure to corticosteroids [20, 21].

While the results of observational cohort studies and retrospective analyses are sensitive to various biases, they sometimes represent the best of our understanding of the evidence, particularly when randomised studies are unavailable. In a large prospective cohort of 4446 infants born at 22 to 25 weeks gestation published by Tyson and colleagues from the Neonatal Research Network of the National Institute of Child Health and Human Development, multivariable analyses showed that those who received intensive care were exposed to antenatal corticosteroids, were of the female sex, were from singleton pregnancies and of higher birth weight had reduced rates of death.[17] In addition, among survivors, the risk of death or impairment at 18–22 months corrected age was also reduced by corticosteroid exposure. Long-term data from the EPICure investigators also showed that antenatal corticosteroids were associated with an increased mental development index assessed at 2.5 and 6 years of age.

Limitation of the study. The limitation of our study was that it was confined to our hospital setting. The generalisation to the community cannot be made. Also, the sample was purposive and not a true representation of the study population. Furthermore, we cannot exclude selection bias in study participation. There was an overrepresentation of individuals with low birth weight among nonparticipants, and such bias may influence the lack of association between exposure and outcome. In addition, our findings do not apply to extremely preterm infants exposed to repeat courses of ACS and born before 28 weeks of gestation.

Prospects for further research:

– The prophylactic use of ACS among preterms in the clinical setting in modern neonatal care has a beneficial magnitude. Antenatal corticosteroids can be given safely in neonates born under 37 weeks to reduce mortality and respiratory morbidity.

– A standardised protocol for administering antenatal corticosteroids in preterms should be brought at the earliest in the country.

– Doctors, Medical professionals, nurses, and primary health care providers should be empowered with knowledge and skills on the importance and use of antenatal corticosteroids in anticipated preterm delivery.

5. Conclusion

The overall incidence of RDS in this study was 30 (15 %), among which 7 (7 %) were exposed to steroids, and 23 (23 %) were not exposed to steroids. Antenatal corticosteroids were significantly associated with reduced incidence of RDS in preterms (neonates born between 28–37 weeks of gestational age). The overall incidence of TTN was found to be 46 (28 %) in this study, among which 14 (14 %) were exposed to steroids, and 32 (32 %) were not exposed to steroids. Antenatal corticosteroids were significantly associated with reduced incidence of TTN in preterms. Antenatal corticosteroids significantly reduce the need for supplemental oxygen, NICU admission, need for CPAP and mortality rate. The dose of antenatal corticosteroids was significantly associated with the incidence of RDS and TTN. 2 doses of steroids reduced RDS and TTN significantly compared to the single dose, which was just significantly associated. This study found no significance between RDS and TTN with gestational age, mode of delivery, birth weight and RDS among steroid-exposed babies. Antenatal corticosteroids were effective in the reduction of morbidity and mortality among premature newborns in the population studied, and therefore their use should be populated. This study emphasises the need to develop quality improvement efforts to optimise appropriate and timely antenatal corticosteroid administration. To obtain more reliable and objective information, further research, including randomised control trials, is necessary.

Conflict of interest

The authors declare that there is no conflict of interest in relation to this paper, as well as the published research results, including the financial aspects of conducting the research, obtaining and using its results, as well as any non-financial personal relationships.

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Data availability

Data will be made available on reasonable request.

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