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Use of Antenatal Corticosteroids prior to Elective Caesarean Section at Term in Reducing the Incidence of Transient Tachypnoea of the Newborn – A ThreeYear Observational Studyin A Premium Institute.

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Abstract:
Background:
Neonates delivered by elective Caesarean section are found to be associated with an increased risk of respiratory morbidity when compared to their vaginal counterparts; and the risk of respiratory complications, mainly respiratory distress syndrome and transient tachypnoea, decreases from 37 weeks to 39 weeks of gestation[1]. The development of respiratory distress leads to admission to a neonatal intensive care unit, separation from the mother, complications from invasive procedures including artificial ventilation and has psychological and financial bearing on the parents.Therefore, Hansen et al concluded that a significant reduction in morbidity would be obtained if elective Caesarean section was deferred to 39 weeks.[2]Antenatal corticosteroids reduce the incidence of respiratorydistress in preterm babies.[3]Studies have been conducted to assess the usefulness of antenatal steroids prior to term Caesareans and have shown a promising outcome with regard to a decrease in incidence of respiratory distress and transient tachypnea of the newborn, thereby suggestive that antenatal corticosteroids may have a role in Caesarean sections planned before 39 weeks of gestation.[4-6]
Objectives: *To study the effect of antenatal corticosteroids in term elective Caesarean section in reducing the incidence of Transient Tachypnea of the Newborn.*
Methodology: *This observational study was conducted at Sri Ramachandra Medical College during the study period of August 2013 – August 2016 with a total of 604 term (37 weeks to 39 weeks) women with singleton pregnancies. Out of the 604 women included, 307 were assigned to Group A (those without steroid administration) and 297 to Group B (those with steroid administration). The steroid used was Injection Betamethasone 12mg, administered 24 hours apart, 24 – 48 hours prior to planned surgery. Neonates were diagnosed with Transient Tachypnoea of the newborn (TTN) if they developed clinical features of respiratory distress like tachypnea along with grunting/ chest retraction/ nasal flaring which resolved within 24 hours of birth, after excluding other possible etiologies of distress like respiratory distress syndrome, pneumonia, meconium aspiration syndrome or pneumothorax by the use of imaging studies or laboratory tests, as indicated.*
Results: *In our study, amongst the 307 neonates in Group A, 49 (15.96%) developed TTN and amongst the 297 in Group B, only 13 (4.3%) developed TTN. There was thus a statistically significant (p value<0.001) decrease in the incidence of TTN amongst the neonates in Group B.*
Conclusion: *The use of antenatal corticosteroids prior to elective Caesarean section at term appears to reduce the incidence of Transient tachypnea in the Newborn.*

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I. Introduction

The rate of Caesarean section in India rose from 8.5% (2005 – 2006) to 17.2% (2015-2016).[7] In Tamil Nadu, the Caesarean section rate increased from 20.3 (2005 – 2006) to 31.4 (2015 – 2016).[8] Contributors to this high Caesarean section rate are the number of high risk pregnancies, change in management of breech and multiple pregnancies, previous Caesareans, conception by artificial reproductive techniques and the number of maternal requests for elective Caesarean section.The increased choice for women at term to undergo a scheduled Caesarean, citing the need for socially convenient times and timed delivery for religious/ superstitious beliefs is also one of the contributing causes.[9]The complications and morbidity issues of Caesarean section in the mother have often been discussed; however, very little attention has been paid to the outcome of the babies born via an elective Caesarean section.

Previous studies have shown elective caesarean section to be associated with an increased risk of respiratory morbidity in neonates when compared to vaginal deliveries; although, methodological shortcomings and differences between studies make it difficult to evaluate properly the causality and magnitude of the association.[2]Other risk factors for respiratory complications include gestational age, mode of delivery, male sex, foetal asphyxia, maternal asthma and diabetes and type of anaesthesia given during delivery (regional or general).[10,11]

The development of respiratory distress leads to admission to a special care baby unit or neonatal intensive care unit, separation from the mother, complications from invasive procedures including artificial ventilationand it was concluded that a significant reduction in morbidity would be obtained if elective Caesarean section was deferred to 39 weeks.[2]

The theories proffered for the development of transient tachypnea of the newborn (TTN) include those that suggest that during labour and birth, corticosteroid production that is increased in the mother and foetus through the stress of labour, encourages the expression of the epithelial channel gene which allows the lung to switch from fluid secretion to fluid absorption, resulting in clearance of lung fluid at birth.[12,13]

Disruption or delay in clearance of the foetal lung fluid results in transient pulmonary oedema that characterizes TTN. Retained fluid accumulates and results in the bronchiolar collapse with areas of air trapping and hyperinflation. These changes result in a net decrease in lung compliance accounting for the clinical manifestations of the condition. It is plausible that these physiological changes associated with labour which are necessary for lung maturation in neonates may not occur in infants delivered by elective caesarean sections.[13]

Respiratory morbidity in cases of term elective caesarean births appears to have a different pathophysiology than in preterm birth; with lack of physiological catecholamine surge and fluid retention in the lungs being the most likely causes.Interestingly, recent evidence indicates that, apart from the traditional mechanical concept of 'vaginal squeeze', molecular mechanisms (predominantly lung epithelial sodium channels) promote alveolar fluid drainage, and these channels may be underactive in foetuses not exposed to the process of labour.[14]Glucocorticoids appear to increase the number and function of sodium channels, as well as the responsiveness to catecholamines and thyroid hormones providing a rationale for their exogenous administration in cases of elective caesarean.

Randomized trials, including a Cochrane review have been carried out regarding maternal administration of steroids before elective caesarean section at term have been sought to evaluate whether giving the recommended dose of corticosteroids before delivery may lead to a reduction in respiratory morbidity in babies.[4,15]When it is necessary to deliver by pre-labour at 37+0-38+6 weeks' gestation, parents can be counseled about the benefits of a single course of antenatal corticosteroids, such as a reduction in respiratory distress.

Opinion is divided on the necessity of antenatal corticosteroids at term, as approximately only 5% of these babies will require admission for respiratory distress and serious morbidity is uncommon. There is also some concern about the potential for long-term adverse effects of corticosteroid exposure in more mature foetuses.[16,17]

This purpose of this observational study was to assess the use of antenatal corticosteroids prior to term elective Caesarean section and to observe its effect on transient tachypnea of the newborn.

II. Materials and Methods

Source: This observational study was conducted at Sri Ramachandra Medical College during the study period of August 2013 – August 2016 with a total of 604 term (37 weeks to 39 weeks) women with singleton pregnancies.

Inclusion criteria:

- Singleton pregnancies
- Gestational age between 37 weeks to 39 weeks
- Age between 20 to 40 years

Exclusion criteria:

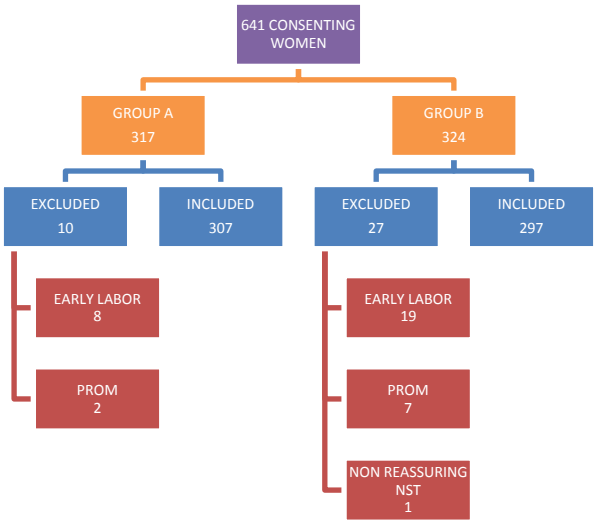
- Multifetal gestation
- HIV Positive, on immunosuppressnts/ known hypersensitity to steroids
- Those who go into spontaneous labour/ PROM
- Features of active systemic infection/ evidence of chorioamnionitis
- Fetus with a lethal or non lethal anomaly
- High risk pregnancies like IUGR, uncontrolled diabetes, severe pre-eclampsia and oligohydramnios

Data thus obtained were analysed and the outcomes were interpreted.

III. Results

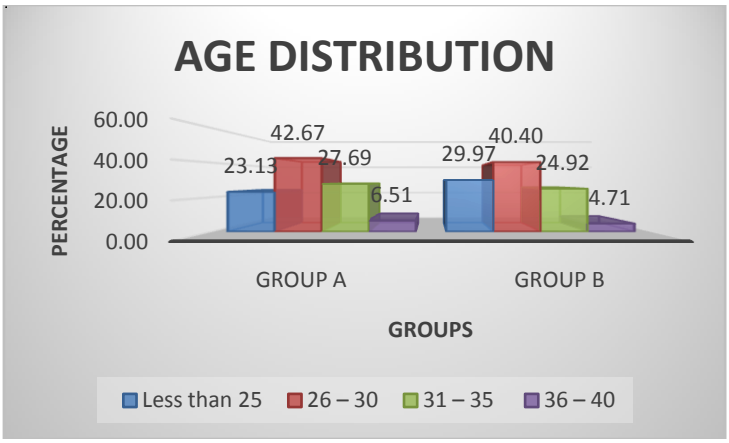
Amongst the 641 women in the study, 604 underwent elective Caesarean and 37 were taken up for emergency Caesarean section; 27 were in view of early labour, 9 because of PROM and 1 due to non - reassuring NST. These patients were excluded from the study as they did not complete their course of steroids.

SCHEME OF PROTOCOL IN STUDY



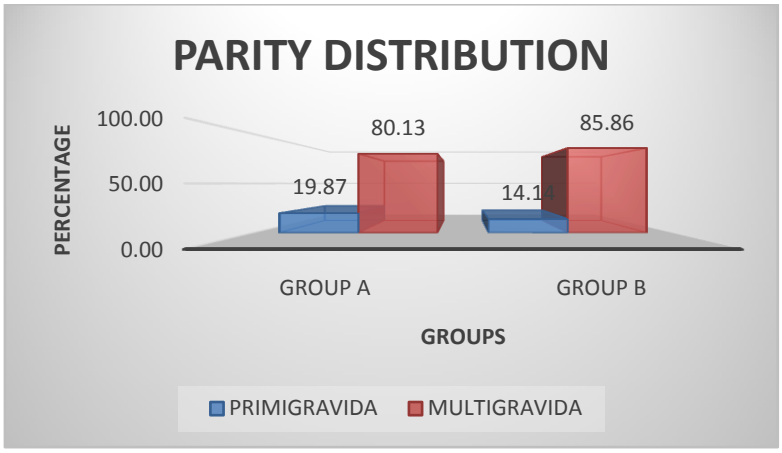
Age distribution

The age of the patients in this study ranged from 20 to 40 years with a mean age of 28.58 (SD ± 3.89) years. The mean age in Group A was 28.95 (SD ± 3.90) years, whereas in Group B, the mean age was 28.22 (SD ± 3.85) years. Majority of the women were in the age group of 26 – 30 years and there was no significant difference in the age distribution between the two groups.



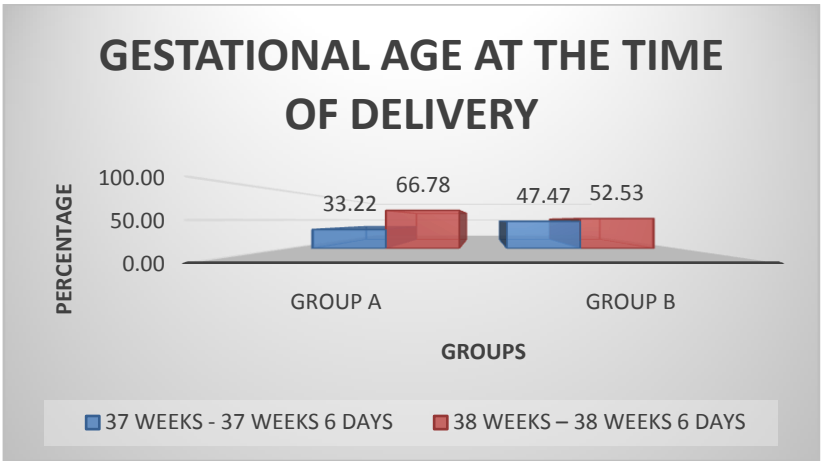
Parity distribution

The total number of primigravida and multigravida in the study were 103 (17.06%) and 501 (82.94%) respectively, with multigravida forming majority of the cases.There was no significant difference in the parity distribution between the two groups.



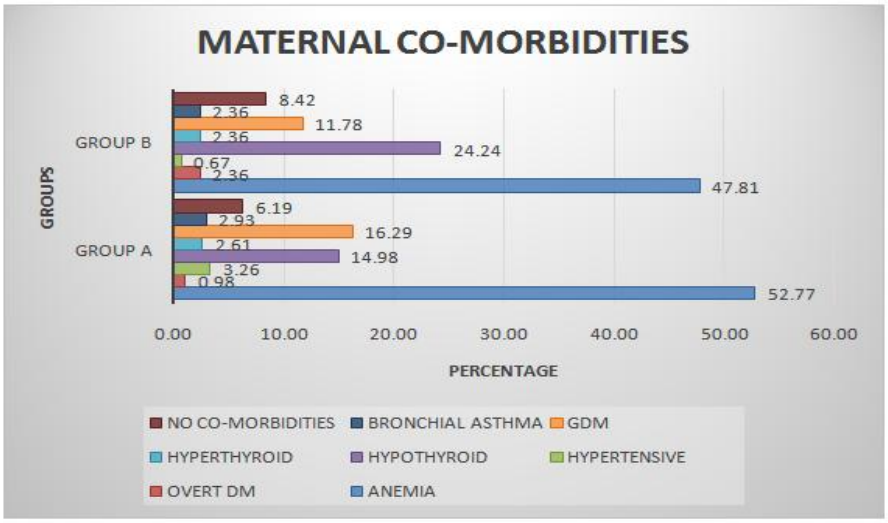
Gestational age at the time of delivery

361 (59.76%) women were between 38 and 38^{+6} weeks of gestational age and 243 (40.24%) of women were between 37 and 37 $^{+6}$weeks of gestational age.There was no significant difference in the gestational age distribution between the two groups.



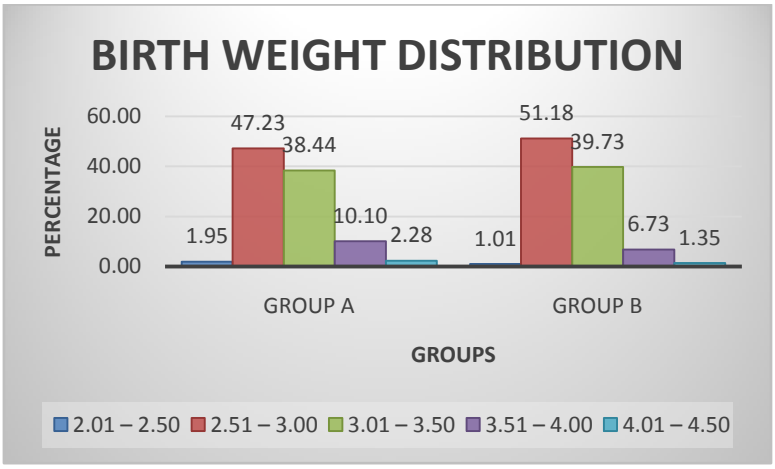
Maternal comorbidities

Out of the women studied, the co-morbidities noted were – anaemia (50.29%), hypothyroidism (19.61%), GDM (14.03%), overt DM (1.67%) hyperthyroidism (2.50%), bronchial asthma (2.54%), gestational hypertension (1.96%). 7.40% of women were found to have no co-morbidities.There was no significant difference in the maternal co-morbidities between the two groups.



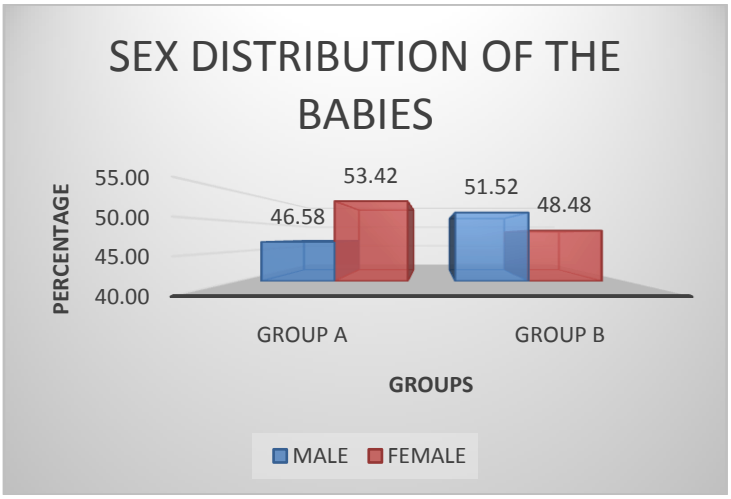
BIRTH WEIGHT

The mean birth weight amongst babies in Group A and Group B was 3.05 kg (SD 0.37) and 2.99 kg (SD 0.35). The mean birth weight amongst all babies included in the study was 3.02 kg (SD 0.36).There was no significant difference in the birth weight distribution between the two groups.



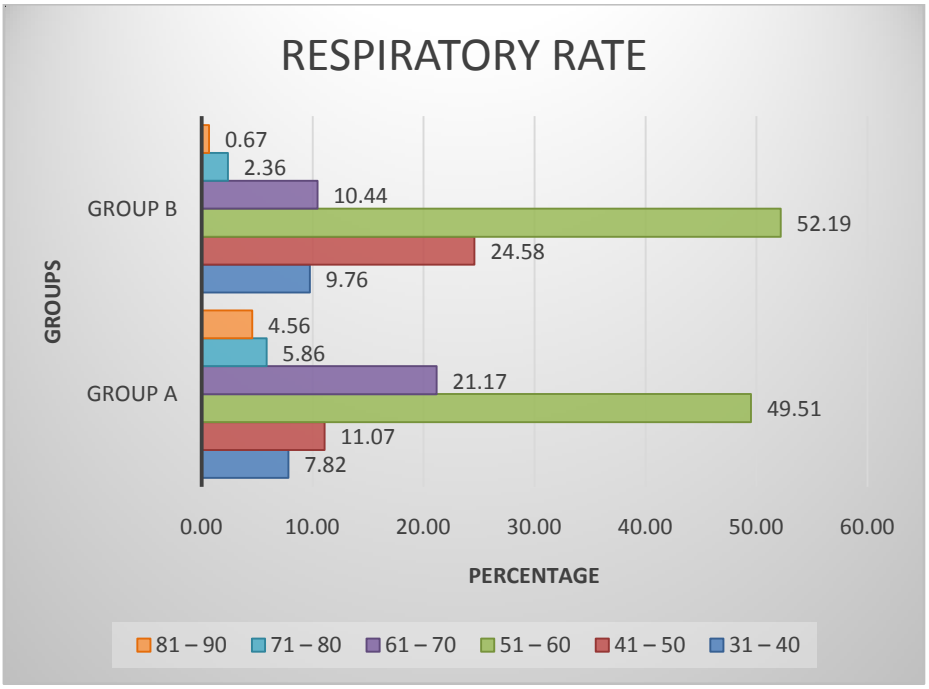
Sex distribution

The number of male babies in the study was 296 (49.1%) and the number of female babies in the study was 308 (50.9%). There was no significant difference in the sex distribution of the babies between the two groups.



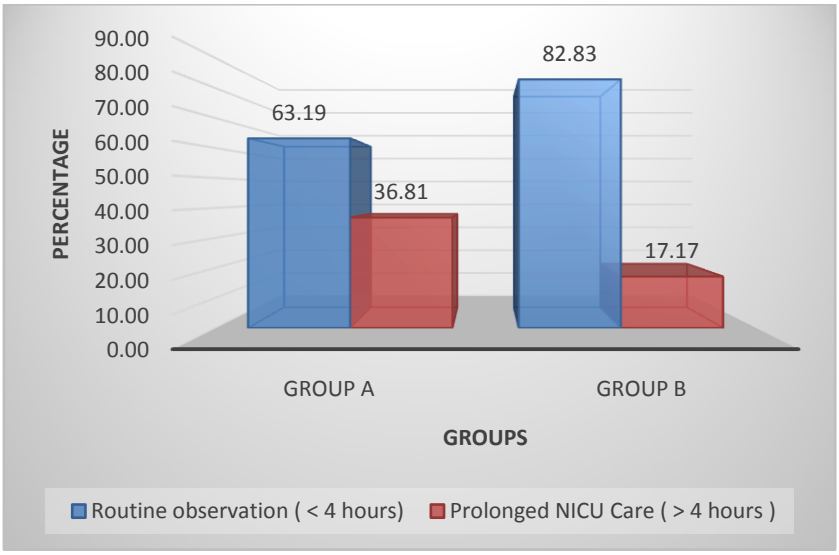
Respiratory rates

The average respiratory rate in the neonates born to the mothers from Group A and Group B were 56.42 and 51.86 respectively.There was a statistically significant (p value 0.000) decrease in the incidence of tachypnea (RR>60) amongst those babies belonging to Group B (13.46%), when compared to those in Group A (31.59%)



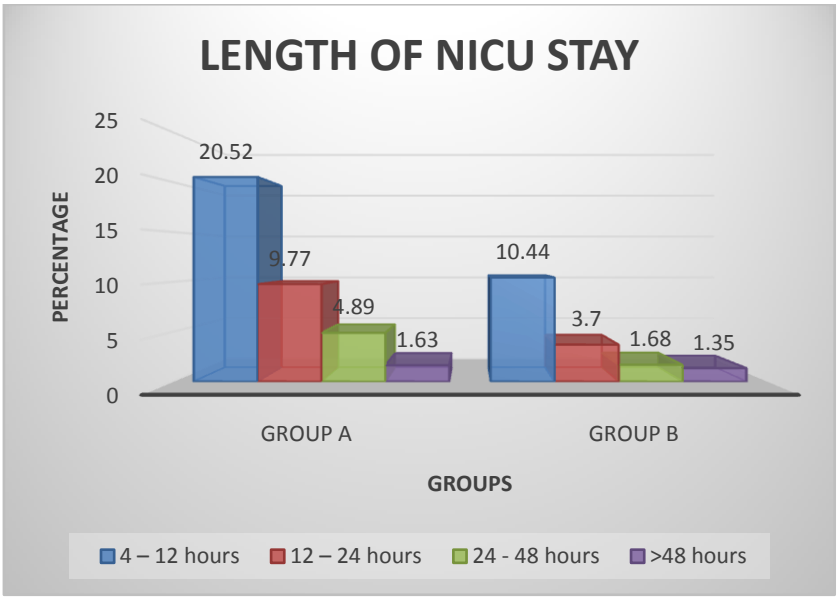
Need for prolonged NICU care

Out of the 604 babies in both groups, 27.15% required prolonged NICU care (> 4 hours); the remaining 72.84% were routinely observed as per hospital protocol. Out of the 307 babies in Group A, 113 (36.8%) required prolonged NICU care; however, out of the 297 babies in Group B, only 51 (17.17%) required the same. This was found to be statistically significant (p value 0.000).



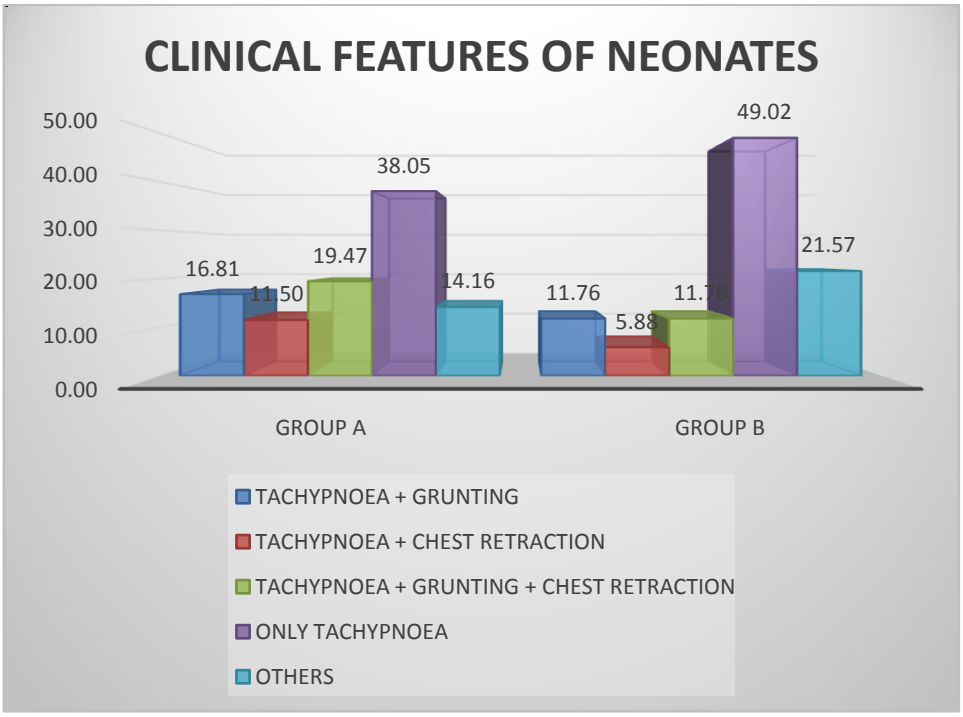
Length of NICU stay

Out of 164 babies admitted for prolonged NICU care in both groups, majority of babies (57.31%) remained in NICU for 4-12 hours. Only 25.02% were admitted for 12 – 24 hours, 12.19% for 24 – 48 hours and 5.48% for >48 hours.There was a statistically significant reduction in the number of hours spent in the NICU by the neonates in Group B, when compared to Group A.



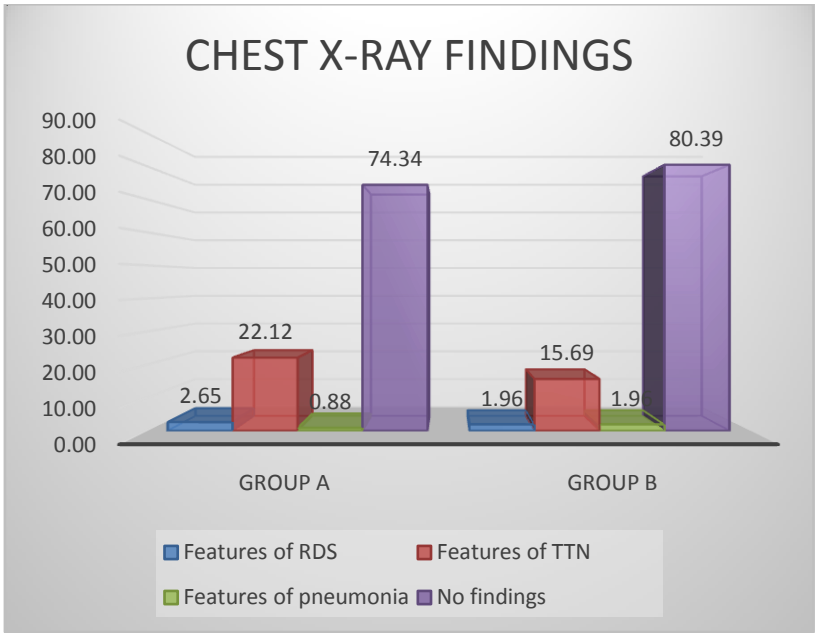
Clinical features of neonates in NICU

Amongst the 164 babies admitted in the NICU, 41.46% had tachypnea without other features of respiratory distress (grunting/ chest retractions) and 42.07% had tachypnea with other features of respiratory distress. 16.47% had clinical features of lethargy (hypoglycaemia), significant meconium stained liquor at birth or hyperbilirubinemia.There was no statistically significant difference (p value 0.27) in the clinical features of the neonates between the two groups



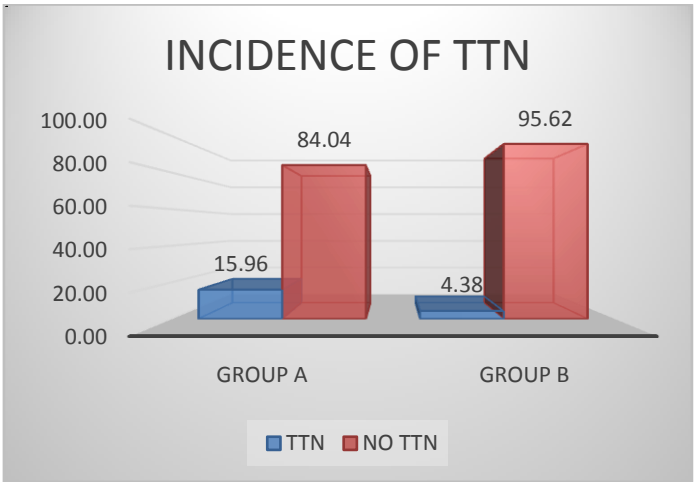
Chest X ray findings

Amongst the 164 babies admitted for prolonged NICU care, 4 (2.43%) had Chest X - ray features of TTN, 33 had features of RDS (20.12%), 2 (1.21%) had features of pneumonia; but majority (76.21%) of them had no significant findings.There was no statistically significant difference (p value 0.73) in the C X- ray findings of the neonates between the two groups



Incidence of TTN

Amongst the 307 babies in Group A, 49 (15.96%) developed TTN and amongst the 297 in Group B, 13 (4.3%) developed TTN. There was a statistically significant (P value 0.000) decrease in the incidence of TTN amongst babies in Group B.



IV. Discussion

Respiratory distress is one of the most important causes of early neonatal morbidity and mortality. In majority of the preterm cases, the cause is primarily attributed to the surfactant deficiency resulting in respiratory distress syndrome. However, in case of term neonates delivered by elective Caesarean section, the reason is primarily attributed to the inadequate absorption of lung fluid which results in the occurrence of Transient tachypnea of the newborn resulting in prolonged NICU stay, maternal separation, need for respiratory support and mechanical ventilation. The use of antenatal corticosteroids for the reduction in respiratory morbidity has been widely studied and its effect on the incidence of respiratory morbidity has been assessed in our study. Our study outcome was compared to the study by Peter Roy Stutchfield et. Al where 19(4%) control babies (N=446) had transient tachypnoea of the newborn compared to 10(2.1%) steroid covered babies (N=373); which concluded that the incidence of transient tachypnoea of the newborn was0.040 in the control group and 0.021 in the treatment group (0.54, 0.26 to1.12) thereby stating that babies born after 37 weeks by elective caesarean section also benefit from antenatal betamethasone, mainly by reducingtransient tachypnoea of the newborn. However, although a decrease inincidence of TTN was noted in this study, a statistical significance was not obtained.[4]

Incidence of TTN in comparison to various studies:

	AHMED ET AL (2015)	Stutchfield et al 2005	Porto et al 2011	Nada et al 2016	Gyamfi – Bannerman et al 2016	PRESENT STUDY
GROUP A (Control)	19.6%	4%	22%	3.4%	9.9%	15.96%
GROUP B (Treatment)	7%	2.1%	24%	1.3%	6.7%	4.38%
P value	0.009	Not Statistically significant	0.77	0.014	<0.01	0.000

Our outcome could also be compared to the study by Ahmed et al 2015, where the main morbidity amongst the neonates was TTN with a finding of 7% of TTN in the study group in comparison to 19.6% in control group, which was statistically significant (p value 0.009)[6]

Quite contradictory to our study, in the study by Porto et al 2011, out of the 143 women who received corticosteroids, 34 (24%) babies developed TTN, in comparison to 29 (22%) in the placebo group (N=130). The rate of transient tachypnoea was high in both groups (P=0.77) and it was ascertained that treatment failed to reduce the incidence of TTN.[18]

In the study by Nada et al 2016, out of 616 neonates in the dexamethasone group, only 8 (1.3%) developed TTN; in comparison to 21 (3.4%) in the control group (N = 611). This was considered statistically significant with a p value of 0.014.[19]

The study by Gyamfi – Bannerman et al 2016 established that amongst the 1427 women who received antenatal betamethasone, only 95 (6.7%) developed TTN; when compared to 138 (9.9%) out of 1400 in the placebo group. This was a statistically significant decrease (p value <0.01 with a relative risk of 0.67 (0.53-0.87) and confidence interval of 95%.[20]

Our study outcome was thus comparable with majority of the above stated various studies, showing a decrease in the incidence of TTN.

V. Conclusion

The use of antenatal corticosteroids (in this study, 2 doses of intramuscular betamethasone given 24 hours apart, 24-48 hours prior to elective Caesarean section) appears to reduce the incidence of TTN. When it is necessary to deliver elective Caesarean section at $37^{+0}$to 38^{+6} weeks' gestation, parents can be counseled about the benefits of a single course of antenatal corticosteroids which has apparent benefit in reducing the respiratory morbidity.

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