



Figure 1: Enrolment, Randomization, treatment and follow-up of patients

## **MEASUREMENT OF KEY VARIABLES**

### **Primary outcome variables**

Presence of neonatal respiratory morbidity. These include respiratory distress syndrome; Transient tachypnea of the newborn and the need for ventilatory support within 72 hours of delivery with supplemental oxygen for at least 2 hours. Any neonate who had any of the 3 conditions is said to have had respiratory morbidity.

### **Secondary Outcome Variables**

These include type of delivery; gestational age at birth; Apgar Scores at first and fifth minutes; admission to the Special Care Baby Unit (SCBU); neonatal hypoglycemia; neonatal jaundice; neonatal sepsis; other neonatal morbidities; length of stay at the hospital; neonatal death within 72 hours of delivery; the need for resuscitation at birth and feeding difficulties.

## **DEFINITIONS**

### **Respiratory Distress Syndrome**

Presence of clinical signs of respiratory distress (tachypnea, chest wall retraction, flaring of the alae nasi, grunting or cyanosis), with a requirement for supplemental oxygen and a chest x ray showing reduced air entry and reticulogranular infiltrates.

### **Transient Tachypnea of the Newborn**

Tachypnea in the absence of chest x ray or with a chest x ray showing normal or increased perihilar interstitial markings resolving within 72 hours.\

## **ADVERSE EVENTS**

To the best of the knowledge of the authors, there were no adverse outcomes recorded in any of the participants.

## **RESULTS**

A total of 286 women fulfilled the inclusion criteria for the study. 143 were randomized to receive dexamethasone (cases) and 143 were randomized to receive placebo (controls). Of these, 34 women were discharged from the hospital during pregnancy and were lost to follow-up, 13 among the cases and 21 among the controls, therefore 130 women remained in the dexamethasone group and 122 in the placebo group with 11.9 % of losses after randomization.

Table 1 shows the socio demographic characteristics of the participants. The mean maternal age of the cases is  $31.2 \pm 4.8$  years while that of the controls is  $30.1 \pm 4.9$  years. These two mean maternal ages showed no statistically significant difference ( $p= 0.55$ ). With respect to occupation, there was no significant difference between the cases and the controls ( $p=0.35$ ). There were no significant differences noted also in the religious beliefs, tribe, and highest level of education of the participants.

**Table 1: Sociodemographic Characteristics of the Cases and Controls**

<b>Variables</b>	<b>Cases N=130</b>	<b>Control N=122</b>	<b><math>\chi^2</math> (p-value)</b>
<b>Maternal age (mean <math>\pm</math>SD)</b>	31.2 $\pm$ 4.8	30.1 $\pm$ 4.9	0.55
<b>Occupation</b>			
Skilled	83(52.9)	74(47.1)	
Semi-skilled	30(46.2)	35(53.8)	1.181(0.55)
Unskilled	17(56.7)	13(43.3)	
<b>Highest level of education</b>			
Primary and below	5(41.7)	7(58.3)	
Secondary	33(45.8)	39(54.2)	2.105(0.35)
Tertiary	92(54.8)	76(45.2)	
<b>Tribe</b>			
Hausa	14(45.2)	17(54.8)	
Igbo	47(53.4)	41(46.6)	
Yoruba	55(55.6)	44(44.4)	(2.729)0.44
Others	14(41.2)	20(58.8)	
<b>Religious belief</b>			
Christianity	76(49.4)	78(50.6)	
Islam	53(54.6)	44(45.4)	(1.609)0.44
Traditional	1(100.0)	0(0.0)	

Table 2 shows the obstetric characteristics of the participants, 59.5% of the cases were booked while 40.5% of the controls were booked and this difference was statistically significant ( $p=0.02$ ). There was no statistically significant difference in the parity, birth weight of the fetus and gestational age at delivery of the cases compared to the controls.

**Table 2: Obstetric Characteristics of the Cases and Controls**

<b>Variable</b>	<b>Cases N=130</b>	<b>Control N=122</b>	<b>P value</b>
<b>Booking status</b>			
<b>Booked</b>	69(59.5)	47(40.5)	<b>0.02</b>
<b>Unbooked</b>	61(44.9)	75(55.1)	
<b>Parity</b>	1(0,2)*	1(0,2)*	0.55
<b>Birth weight in grammes</b>	2974.61(±453.29)	2945.90(±561.15)	0.65
<b>GA at Delivery</b>	35.68(±0.93)	35.75(±0.94)	0.51

\*Median(inter quartile range)

Table 3 shows the Incidence of respiratory morbidity among the cases and controls. Any neonate who had any of the 3 primary outcome measures viz respiratory distress syndrome, transient tachypnea of the newborn or need for ventilatory support is said to have had a respiratory morbidity. The risk for the occurrence of at least one type of respiratory morbidity was significantly lower in those that received corticosteroid compared to those that did not receive. (OR= 0.12, 95% C.I =0.04 – 0.31, P=0.00003). Corticosteroid administration was associated with significant reduction in the rate of respiratory distress syndrome (O.R=0.27, 95% C.I=0.08 – 0.84, p=0.032), Transient tachypnea of the newborn(O.R=0.11, 95% C.I=0.02 – 0.49, p=0.0016), and need for ventilatory support (O.R=0.15, 95% C.I=0.05 – 0.39, p=0.00006).

**Table 3: Incidence of Respiratory morbidity among cases and controls**

Variables	Cases N=130	Control N=122	Odds ratio	95% C.I	p-value
Respiratory Morbidity					
Yes	5(3.8)	31(25.4)	0.12	0.04 – 0.31	0.000003*
No	125(96.2)	91(74.6)	Ref	Ref	
Respiratory distress syndrome					
Yes	3(3.1)	13(10.7)	0.20	0.06 - 0.69	0.032*
No	127(96.9)	109(89.3)	Ref	Ref	
Transient tachypnea of newborn					
Yes	2(1.5)	15(12.3)	0.11	0.02 – 0.49	0.0016*
No	128(98.5)	107(87.7)	Ref	Ref	
Need for ventilatory support					
Yes	5(3.8)	26(21.3)	0.15	0.05 - 0.39	0.00006*
No	125(96.2)	96(78.7)	Ref	Ref	

\*Significant p-value

Table 4 shows the association of other non-respiratory neonatal complications with dexamethasone use. Corticosteroid administration did not significantly affect the risk of hypoglycaemia, neonatal sepsis, neonatal jaundice, neonatal death and feeding difficulties. Corticosteroid use however significantly reduced the risk of birth asphyxia (O.R = 0.25, 95% C.I = 1.57 – 10.47, p= 0.004), admission to neonatal intensive care unit (O.R= 0.41, 95% C.I= 0.21 – 0.78, p=0.009) and need for active resuscitation at birth(O.R =0.31, C.I= 0.12 – 0.76, p=0.014).

**Table 4: Bivariate analysis of other neonatal complications among cases and controls**

Variables	Cases N=130	Controls N=122	Odds ratio	95% C.I	p-value
<b>Birth Asphyxia</b>					
Yes	6(4.6)	20(16.4)	0.25	0.10 – 0.63	0.004*
No	124(95.4)	102(83.6)	Ref	Ref	
<b>NICU admission</b>					
Yes	17(13.1)	33(27.0)	0.41	0.21 - 0.78	0.009*
No	113(86.9)	89(73.0)	Ref	Ref	
<b>Hypoglycemia</b>					
Yes	10(7.7)	10(8.2)	0.93	0.38 – 2.28	0.93
No	120(92.3)	112(91.8)	Ref	Ref	
<b>Neonatal sepsis</b>					
Yes	10(7.7)	11(9.0)	0.84	0.35 – 2.02	0.88
No	120(92.3)	111(91.0)	Ref	Ref	
<b>Neonatal jaundice</b>					
Yes	9(6.9)	10(8.2)	0.83	0.33 – 2.08	0.89
No	121(93.1)	112(91.8)	Ref	Ref	
<b>Neonatal death</b>					
Yes	2(1.5)	4(3.3)	0.46	0.10 - 2.21	0.62
No	128(98.5)	118(96.7)	Ref	Ref	
<b>Need for resuscitation at birth</b>					
Yes	7(5.4)	19(15.6)	0.31	0.13 – 0.75	0.014
No	123(94.6)	103(8.4)	Ref	Ref	
<b>Feeding difficulties</b>					
Yes	1(0.8)	3(2.5)	0.31	0.04– 2.22	0.58
No	129(99.2)	119(97.5)			

Table 5 shows the association between maternal factors and the occurrence of respiratory morbidity in the neonate. The presence of hypertension, preterm labour, pre labour rupture of membranes and antepartum haemorrhage had no significant effect on respiratory morbidity.

Delivery by caesarean section compared to vaginal delivery (O.R= 2.11, 95% C.I of 1.01 – 4.44, p=0.04) and presence of diabetes mellitus (O.R=4.12, 95% C.I= 1.59 – 10.71, p=0.0054) significantly increased the risk of respiratory morbidity.

**Table 5: Bivariate association between maternal factors and effect on respiratory morbidity**

Variable	Respiratory morbidity		Odds Ratio	95% C.I	P value
	Yes (n=36)	No (216)			
	Yes	No			
<b>Route of delivery</b>					
Caesarean section	24(18.6)	105(81.4)	2.11	1.01 – 4.43	0.04
Vagina delivery	12(9.8)	111(90.2)	Ref		
<b>Hypertension</b>					
Yes	13(15.3)	72(84.7)	1.13	0.54 – 2.36	0.89
No	23(13.8)	144(86.2)	Ref		
<b>Diabetes Mellitus</b>					
Yes	8(36.4)	14(63.6)	4.12	1.59 – 10.71	0.0054
No	28(12.2)	202(87.8)	Ref		
<b>Preterm Labour</b>					
Yes	2(5.3)	36(94.7)	0.29	0.07 – 1.26	0.14
No	34(15.9)	180(84.1)	Ref		
<b>Pre-labour rupture of membranes</b>					
Yes	2(4.9)	39(95.1)	0.27	0.06 – 1.14	0.10
No	34(16.1)	177(85.1)	Ref		
<b>Ante partum haemorrhage</b>					
Yes	6(11.8)	45(88.2)	0.76	0.30 – 1.92	0.72
No	30(14.9)	171(85.1)	Ref		



Table 6 shows the multiple logistic regression analysis of factors which had significant effects on respiratory morbidity. After correcting for presence of diabetes mellitus and delivery by caesarean section, corticosteroid administration to the mother at risk of late preterm delivery reduced the risk of respiratory morbidity almost 9-fold (AOR= 0.11, 95% C.I= 0.04 – 0.31,  $p < 0.00001$ )

**Table 6: Multiple logistic regression analysis of Corticosteroid administration as an independent determinant of Respiratory morbidity**

Variable	AOR	95% C.I	p value
Corticosteroid administered	0.11	0.04 – 0.31	0.0000
Diabetes mellitus	4.46	1.50 - 13.29	0.0071
Cesarean section	2.12	0.96- 2.16	0.0626

AOR= Adjusted odds ratio

