

## ORIGINAL RESEARCH ARTICLE

# Antenatal corticosteroid and early neonatal outcomes among preterm neonates delivered at a tertiary hospital in Tanzania

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## Abstract

Antenatal corticosteroids (ACS) have been proven to reduce prematurity-related neonatal complications and deaths. Tanzania introduced national ACS guidelines in 2015 with immediate adoption in tertiary facilities. This study aimed to assess the effect of ACS exposure among preterm neonates delivered at Muhimbili National Hospital. A cross-sectional study was conducted between August 2017 and January 2018, where 160 preterm neonates with their mothers were recruited and their data was collected. We used univariate and bivariate logistic regression analysis to determine associations between ACS exposure and adverse neonatal outcomes. ACS exposure significantly reduced the risk of respiratory distress syndrome (RDS) by 58% (COR=0.42, 95% CI, 0.2-0.8, p<0.01) and neonatal death by 75%, (COR=0.25, 95% CI, 0.1-0.8, p=0.01). There was no effect on neonatal sepsis or necrotizing enterocolitis. We conclude that exposure to ACS was significantly associated with reduced RDS and mortality among preterm neonates. (*Afr J Reprod Health* 2023; 27 [7]: 23-31).

**Keywords:** Antenatal corticosteroids, Preterm neonates, early neonatal outcome

## Résumé

Il a été prouvé que les corticostéroïdes prénatals (SCA) réduisent les complications et les décès néonataux liés à la prématurité. La Tanzanie a introduit des lignes directrices nationales sur l'ACS en 2015 avec une adoption immédiate dans les établissements tertiaires. Cette étude visait à évaluer l'effet de l'exposition au SCA chez les nouveau-nés prématurés nés à l'hôpital national de Muhimbili. Une étude transversale a été menée entre août 2017 et janvier 2018, où 160 nouveau-nés prématurés avec leurs mères ont été recrutés et leurs données ont été recueillies. Nous avons utilisé une analyse de régression logistique univariée et bivariée pour déterminer les associations entre l'exposition aux SCA et les issues néonatales indésirables. L'exposition aux SCA a réduit de manière significative le risque de syndrome de détresse respiratoire (SDR) de 58 % (COR = 0,42, 95 %, IC, 0,2-0,8, p <0,01) et de décès néonatal de 75 %, (COR = 0,25, 95 %, IC, 0,1-0,8, p=0,01). Il n'y a eu aucun effet sur la septicémie néonatale ou l'entérocolite nécroisante. Nous concluons que l'exposition au SCA était significativement associée à une réduction du SDR et de la mortalité chez les nouveau-nés prématurés. (*Afr J Reprod Health* 2023; 27 [7]: 23-31).

**Mots-clés:** Corticostéroïdes anténatals, nouveau-nés prématurés, évolution néonatale précoce

## Introduction

Globally, eleven per cent of all babies are born preterm, with great variations between and within the regions<sup>1</sup>. Preterm birth is defined as the birth of a live baby before 37 completed weeks of pregnancy and is further classified as extreme preterm (<28 weeks of gestation), very preterm (28-32 weeks) and moderate to late preterm (32 to 37 weeks)<sup>2</sup>. Prematurity accounts for a third of neonatal death and 16% of all under-five deaths globally, with over 80% of these deaths occurring

in Africa and South Asian countries<sup>1-5</sup>. Tanzania is among the ten countries with the highest rates of preterm birth reported to be between 11-16%<sup>4,5</sup>. Several risk factors have been associated with preterm births; extremes of maternal age, a short inter-pregnancy interval of ≤24 months, prior preterm birth, multiple pregnancies, premature membrane rupture, maternal co-morbid conditions and poor antenatal care<sup>4,6-9</sup>.

Prematurity is associated with immediate life-threatening complications such as respiratory distress syndrome (RDS), intraventricular

haemorrhage (IVH), necrotizing enterocolitis (NEC), neonatal sepsis and neonatal death<sup>4,10,11</sup>. RDS is the most common preterm complication resulting from an incomplete physiological process that occurs in the last trimester where type II pneumocytes mature to type I cells responsible for surfactant production and alveolar formation. Consequently, preterm babies <34 weeks have surfactant deficiency and poorly developed respiratory units causing respiration-perfusion mismatch and present with hypoxia, hypercapnia and acidosis<sup>12</sup>. The severity of RDS complications is related to the level of prematurity. Corticosteroids given antenatally stimulate fetal lung maturation and surfactant production and reduce the risk and severity of RDS<sup>13,14</sup>.

The World Health Organization (WHO) with other professional bodies recommends the use of antenatal corticosteroid (ACS) therapy in anticipated preterm labour with other interventions such as the use of tocolytics and antibiotics for specific at-risk women<sup>15-17</sup>. However, these recommendations are not always adhered to. Challenges include the availability of the essential drugs, knowledge and practice of health workers and other inconsistencies in health systems<sup>18,19</sup>. For ACS, most studies report that exposure to a single course of ACS significantly reduced death, RDS, NEC, and neonatal sepsis in preterm neonates delivered from the GA  $\geq 24$  to < 34 weeks<sup>14,16,17,20,21</sup>. There is a significant reduction of RDS up to 50%, neonatal death, NEC, and neonatal sepsis once delivery of preterm neonates occurs from  $\geq 24$  hours and  $\leq 7$  days after exposure to a single complete course of ACS. The optimal benefit of ACS occurs when delivery occurs 24 to 48 hours after completion of a single course of ACS<sup>14,20,22</sup>. Other studies reported conflicting results that the benefit of ACS can be seen even if, preterm birth occurs more than 7 days. Despite evidence of the proven benefit of ACS on specific neonatal conditions like RDS and deaths, there are still concerns about the use of ACS in the presence of maternal infection, the benefits of repeated doses of ACS and the time from administration to delivery<sup>14</sup>.

The Muhimbili National Hospital (MNH) adopted the use of the Ministry of Health Antenatal Corticosteroids for preterm labour guidelines launched in 2015<sup>23</sup>.

There has been no documentation on the early neonatal outcomes of preterm neonates exposed to a full course of ACS. This study aimed to assess the effect of ACS exposure on preterm neonates delivered at a tertiary national hospital, MNH.

## Methods

### Study design

A cross-sectional study comparing adverse neonatal outcomes of preterm neonates based on their ACS exposures.

### Study setting

This study was done at MNH, a tertiary and teaching hospital affiliated with the Muhimbili University of Health and Allied Sciences (MUHAS). The hospital has the largest Neonatology Unit in Dar es Salaam and the Coastal region. The unit is hosted in the maternity building and includes a small neonatal intensive care unit (NICU) equipped with nasal Continuous Positive Airway Pressure ventilation (CPAP) for RDS. The Neonatology Unit has 148 cots with an estimated 560 monthly admissions, 75% of these neonates are delivered at MNH, and the rest are neonates referred from other health facilities. The Neonatal Unit has four rooms dedicated to premature babies, grouped by birth weight (600g to 1800g, 1900g to 2500g) and the level of support required (NICU). The unit has one neonatologist, five specialists, one registrar, 24 nurses, residents and intern doctors providing routine and emergency services.

The hospital receives an average of 180 pregnant women with anticipated preterm births per month: approximately two-thirds originate from MNH and a third are referrals from other hospitals. Once admitted to the maternity ward, women are reviewed by the on-call team that comprises consultants, specialists, residents, intern doctors and nurses. Women with anticipated preterm birth are given ACS with other management as required.

During the study period, the hospital adopted the Ministry of Health and Social Welfare guidelines on the administration of ACS for preterm labour, which recommends the use of Dexamethasone 6mg intramuscularly, given at 12-hour intervals for 48 hours<sup>23</sup>. Betamethasone, another corticosteroid given 12mg every 24 hours

for two doses is not used routinely in the country, although it is also in the national guidelines.

### Study population

Women who had preterm birth at MNH with their preterm neonates of gestation age from  $\geq 28$  to  $< 37$  weeks. Preterm neonates whose mothers received the full course of ACS therapy (intramuscular Dexamethasone injection 6mg 12-hourly for 48 hours) were identified as ACS-exposed preterm neonates. Those whose mothers did not receive, or did not complete the full dose were identified as ACS-unexposed. Exclusion criteria were stillbirth, major congenital anomaly incompatible with life, and women and preterm neonates whose ACS was not initiated at MNH and could not ascertain the correct dose of ACS.

### Sample size

The sample size was calculated using two proportions, 18% and 42% of preterm neonates who develop RDS among ACS-exposed and ACS-unexposed groups respectively. The proportions were obtained from a study by Guruvare et al 2015 at a tertiary-level teaching hospital in Kasturba Medical College, New Delhi, India<sup>24</sup>. E. Whitley formula was used to calculate the sample size required to compare different proportions in two equal-sized groups<sup>25</sup>. The sample size for exposed and unexposed preterm neonates to ACS was in a ratio of 1:1.

$$n = \frac{[p_1(1-p_1) + p_2(1-p_2)]}{(p_1 - p_2)^2} \times C_{p, power}$$

$$n = \frac{[0.18(1-0.18) + 0.42(1-0.42)]}{(0.18 - 0.42)^2} \times 10.5$$

$$n = \frac{[0.18(1-0.18) + 0.42(1-0.42)]}{(0.18 - 0.42)^2} \times 10.5 = 79.8 \approx 80$$

Total sample size.  $N = 2n$ ,  $N = 2 \times 80 = 160$   
 $n$  =, represent the sample size required to be taken from ACS exposed and unexposed preterm neonates,  $P_1$  and  $P_2$  = proportions of preterm neonates exposed and unexposed to antenatal corticosteroids respectively  $C_p$ , power = 10.5, at a  $p$ -value of  $< 0.05$ , 95% confidence level and power of the study of 90%.

### Sampling technique

All eligible mothers and their preterm neonates exposed and unexposed to ACS delivered at MNH

were consecutively recruited in the study until the desired sample size was achieved.

### Data collection

Data collection was done between August 2017 and January 2018. Preterm neonates were identified daily, and their gestation age was calculated according to the first date of last normal menstruation or early fetal ultrasound and counterchecked with neonatal assessment using the New Ballard score<sup>26</sup>. If the difference was greater than one week, or if the woman was not sure of the first date of her last menstruation, the final gestation age was based on the New Ballard score.

Eligible mother-neonate pairs were recruited and followed up until discharge. Preterm neonates' exposure to ACS was confirmed retrospectively through maternal medical records from the admission files. Unexposed preterm neonates were recruited from referred pregnant women, whom antenatal corticosteroid was not initiated at their primary health facilities and arrived at MNH in the active phase of labour and delivery occurred before the re-initiation of the ACS as confirmed through maternal referral note. The first author interviewed mothers, reviewed antenatal, intrapartum and postpartum medical records and discharge forms, and abstracted this information into the study questionnaire.

The investigating team followed up with the preterm neonates in their respective admission wards and reviewed medical records daily. Mother-neonate pair who were discharged before completing the seventh day of life were followed up by telephone calls. Follow-up was terminated if neonatal death occurred before the 7<sup>th</sup> day of life.

### Study variables

Independent variables collected were maternal demography, obstetric history, medical history, intrapartum history and early postpartum history, including the use of tocolytics. Neonatal information collected were gestation age (GA) at delivery, mode of delivery, whether ACS was completed, delivery interval and cause of preterm delivery. Dependent variables were the occurrence of any complication related to prematurity or a composite outcome with one or more complications of prematurity as shown in Box 1.

**Box 1:** Clinical criteria for assessment of preterm neonatal outcomes

Outcome variable	Clinical diagnosis
Respiratory distress syndrome [RDS]	tachypnoea, nasal flaring, intercostals and sterna retraction, grunting, cyanosis, use of oxygen and intubation.
Necrotising Enterocolitis [NEC]	abdominal distension, rectal bleeding or blood-stained stools, bilious drainage from nasal gastric tubes, vomiting and diarrhoea
Neonatal Sepsis	temperature $\geq 38^{\circ}\text{C}$ and evidenced-based diagnosis of neonatal sepsis documented in the patient files, including clinical assessment based on the standard WHO criteria and are done investigations done if.
Death	cause of death was based on doctors' diagnosis from the medical case note and neonatal unit record
Composite outcome	Any one or more adverse outcomes in a preterm neonate

**Data management and analysis**

Data were coded, entered and analyzed in SPSS Statistics version 23. Descriptive analysis was done on the maternal social demographic, obstetrics and preterm neonates' characteristics, whereby categorical variables were summarized using proportions and presented in tables. Maternal age was grouped into <20 years, 20 to <35 years and  $\geq 35$  years. Preterm neonates were further classified as very preterm (GA 28-33<sup>+6</sup> weeks) and moderate to late preterm with (GA 34 - 37 weeks). Four primary variables namely RDS, NEC, Sepsis and Death were computed. A secondary composite variable was computed from four primary composite variables to assess the overall outcome of preterm. Bivariate logistic regression was done to assess the association and strength of association between independent variables and dependent primary and secondary composite variables. Crude odd ratio (COR) at 95% confidence level with p-value <0.05 and confidence interval (CI) which doesn't include 1 were considered statistically significant. The chi-square test and Fisher's exact test were used in the analysis.

**Ethical issues**

Ethical clearance for this study was obtained from Senate Research and Publication Committee at the Muhimbili University of Health and Allied Sciences (MUHAS). Permission to conduct the study was sought from the Executive Director of Muhimbili National Hospital.

**Results**

During the six-month study period, 419 of the 3082 deliveries (13.6%) at MNH were preterm deliveries.

One hundred-sixty mother-neonate pairs were recruited in the study, 80 in ACS exposed and 80 in ACS unexposed neonates. Dexamethasone was the only antenatal corticosteroid used. A full course of ACS consisted of four doses of was intramuscular injection of Dexamethasone 6mg given 12-hourly for 48 hours.

Table 1 shows socio-demographic and obstetric characteristics among women who delivered prematurely. Overall, over 80% of women with preterm deliveries were in the 20-34 years age group. Approximately half had secondary education or above, and 68% were self-employed or employed. Primiparous women were approximately a third (29.4%) of all women with preterm birth. Fifty-seven percent of all women with preterm birth had gestation age between 28-34 weeks. Among the preterm births, 38% had spontaneous preterm labour, 31.9% had premature pre-labour rupture of membranes, and 41% had twin pregnancies.

Maternal age category, marital status, education and parity were not different in those who were exposed or not exposed to ACS. Compared to ACS-unexposed women, a higher proportion of women who were ACS-exposed reported to be employed. The difference was statistically significant (self-employed 62% vs. 48.8% and employed 18.8% vs 7.5% in ACS-exposed and ACS-unexposed respectively, p-value < 0.01). Of the ACS-exposed women, a higher proportion was of lower gestation age and were delivered by caesarian section (52.2% vs 26.2%, p-value < 0.01) compared to ACS-unexposed women. Over eighty per cent of ACS-exposed women had a documented obstetric complication such as premature membrane rupture, preeclampsia and others such as placenta previa (82% vs 40%, p-value <0.01) as shown in Table 1.

**Table 1:** Social-demographic and obstetric characteristics in the two study groups (N=160)

Variables	ACS Exposure status			p-value
	ACS-exposed n (%)	ACS-unexposed n (%)	All n (%)	
<b>Maternal age in years</b>				
< 20	2 (2.5)	6 (7.5)	8 (5.0)	0.2
20-34	65 (81.2)	66 (82.5)	131 (81.9)	
>=35	13 (16.0)	8 (10.0)	21 (13.1)	
<b>Marital status</b>				
Single	21 (26.2)	22 (27.5)	43 (26.9)	0.22
Married/cohabiting	59 (73.8)	58 (72.5)	117 (73.1)	
<b>Occupation</b>				
Employed	15 (18.8)	6 (7.4)	21 (13.1)	<0.01
Unemployed	15 (18.8)	35 (43.8)	50 (31.3)	
Self-employed	50 (62.4) **	39 (48.8)	89 (55.6)	
<b>Education Level</b>				
No formal	2 (2.5)	4 (5.0)	6 (3.8)	0.73
Primary	39 (48.8)	40 (50.0)	79 (49.4)	
Secondary and above	39 (48.8)	36 (45.0)	75 (46.9)	
<b>Parity</b>				
Para 1	19 (23.8)	28 (35)	47 (29.4)	0.13
Para 2-4	50 (62.5)	47 (58.8)	97 (60.6)	
Para ≥5	11 (13.8)	5 (6.3)	16 (10)	
<b>Gestation age in weeks</b>				
28-<34	51 (63.7)	41 (51.2)	92 (57.5)	0.11
34-<37	29 (36.3)	39 (48.8)	68 (42.5)	
<b>Type of pregnancy</b>				
Single	61 (76.2)	33 (41.2)	94 (58.8)	<0.01
Twin	19 (23.8)	47 (58.8)	66 (41.2)	
<b>Maternal diagnosis</b>				
Spontaneous labour	14 (17.5)	48 (60.0)	62 (38.8)	<0.01
PPROM	30 (37.5)	21 (26.2)	51 (31.9)	
Pre-eclampsia	29 (36.3)	4 (5.0)	33 (20.6)	
Others*	7 (8.8)	7 (8.8)	14 (8.8)	
<b>Mode of delivery</b>				
Vaginal birth	38 (47.5)	59 (73.8)	97 (60.6)	<0.01
Cesarean birth	42 (52.5)	21 (26.2)	63 (39.4)	

\*Oligohydramnios, placenta previa, abruption placenta, anaemia, eclampsia, cervical incompetence, HELLP syndrome and recurrent fetal loss; PPROM; preterm premature rupture of membrane

**Table 2:** Preterm neonates' characteristics and their exposure status (N= 160)

Variables	ACS Exposed n (%)	ACS Unexposed n (%)	Total (N=160)	P value
<b>Required Oxygen</b>				
Yes	33 (41.2)	50 (62.5) **	83 (51.9)	<0.01
No	47 (58.8)	30 (37.5)	77 (48.1)	
<b>CPAP use</b>				
Yes	8 (10.0)	21 (26.2) **	29 (18.1)	<0.01
No	72 (90.0)	59 (73.8)	131 (81.9)	
<b>NICU admission</b>				
Yes	20 (25.0)	26 (32.5)	46 (28.8)	0.3
No	60 (75.0)	54 (67.5)	114 (71.2)	
<b>Apgar scored at 5 minutes</b>				
<7	5 (6.2)	11 (13.8)	16 (10)	0.1
≥7	75 (93.8)	69 (86.3)	144 (90)	

CPAP; continuous positive air pressure ventilation; NICU; neonatal intensive care unit

\*\*p-value < 0.01

**Table 3:** Effects of ACS exposure on the development of RDS, NEC, Sepsis and Death

Variables	Categories	Outcome variables		COR (95%)	p-value
		Yes	No		
RDS					
ACS Exposure status	Exposed (n=80)	32(39.5%)	48(60.8%)	1	<0.01
	Unexposed(n=80)	49(60.5%)	31(39.2%)	0.42(0.2-40.8)	
NEC					
ACS Exposure status	Exposed(n=80)	2(2.5%)	78(97.5%)	1	0.68*
	Unexposed(n=80)	4(5%)	76(95%)	0.49(0.1-2.7)	
SEPSIS					
ACS Exposure status	Exposed(n=80)	11(13.8%)	69(86.3%)	0.5(0.2-1.4)	0.2
	Unexposed(n=80)	6(7.5%)	74(92.5%)	1	
DEATH					
ACS Exposure status	Exposed(n=80)	4(5%)	76(95%)	1	0.01
	Unexposed(n=80)	14(17.5%)	66(82.5%)	0.25(0.1-0.8)	

\*Fisher’s exact test; RDS; respiratory distress syndrome; NEC; necrotizing enterocolitis

**Table 4:** Composite adverse neonatal outcome by ACS exposure status (N=160)

Neonate’s status	Total (N=160)	ACS exposure status		COR (95%)	p value
		Exposed n (%)	Unexposed n (%)		
Neonatal outcome					
Good	80(50)	42(52.5)	28(35)	0.49 (0.26-0.92)	0.026
Poor	80(50)	38(47.5)	52(65)	1	

ACS; antenatal corticosteroids

Table 2 shows preterm neonate clinical characteristics at birth including Apgar score, need for respiratory support and NICU admission. A lower proportion of ACS-exposed preterm neonates required oxygen therapy (41.2% VS 62.5%, p-value < 0.01) or continuous positive air pressure ventilation (CPAP) (10.0% vs 26.0%, p-value 0.01) compared to the ACS-unexposed group. There was no statistical difference in the proportion of neonates admitted to NICU or having low Apgar score ( $\leq 7$  at 5 minutes) between the two groups. Table 3 shows neonatal outcomes in the first 7 days of life by ACS exposure group. Preterm neonates that were exposed to ACS showed a significantly reduced risk of RDS and Death by 58% (COR=0.42, 95%, CI, 0.2-0.8, p<0.01) and 75% (COR=0.25, 95%, CI, 0.1-0.8, p= 0.01) respectively compared to those who were not exposed to ACS. There was no significant difference in the incidence of NEC and neonatal sepsis among the two preterm neonates who were ACS-exposed and those who were ACS un-exposed. Overall, preterm neonates that were exposed to ACS had significantly reduced overall adverse neonatal outcome by 51%, (COR =0.49, 95%, CI 0.26-0.92, p=0.026) as shown in Table 4.

## Discussion

This study assessed the clinical outcomes of preterm neonates exposed to a complete dose of ACS at a tertiary teaching hospital in a low- and middle-income country. Our findings indicated that ACS-exposed preterm neonates were less likely to develop RDS, death, or a composite adverse neonatal outcome. We did not observe any difference in neonatal sepsis or NEC between the two groups. Our study shows that ACS is beneficial in reducing RDS, which is the commonest complication and cause of death among preterm neonates. This finding adds to several literatures that have shown the benefits of ACS, especially among extreme preterm neonates. Few studies in low and middle-income countries have reported no benefit in reducing RDS<sup>18,19</sup>. These studies have specifically acknowledged that reasons for non-benefit were related to other challenges around the use of ACS, such as inconsistency in health systems to support the correct use of ACS. These include correct estimation of gestation age, different guidelines, low availability and incomplete dosages. There are also issues around the efficacy time, and correct selection of women to receive

ACS as well as policies in place to support appropriate use<sup>18 19</sup>. For example, the selection of women to receive ACS is a difficult decision due to unavailable tests to correctly diagnose imminent preterm delivery in most LMICs.

We also found that approximately a third of women given ACS were between 34-36<sup>+7</sup> gestation weeks. Literature shows unequivocal advantages of ACS on RDS at lower gestation age, however, the benefits of administering ACS for late preterm neonates (between 34-36<sup>+7</sup>) is still unclear. Gyamfi-Bannerman (2016) reported that the administration of ACS between 34-36<sup>+7</sup> is beneficial in reducing RDS in late preterm neonates<sup>27</sup>, while other authors have advised doing so in this age group should be done with caution<sup>28,29</sup>. In this study, we did not investigate the effect of gestation age on the different neonatal outcomes.

This study showed no significant difference between ACS-exposed and ACS-unexposed preterm neonates in the rate of NEC or neonatal sepsis. Necrotizing enterocolitis has a very intricate pathway and includes stasis of food, gut function, bacterial colonization, blood circulation mode of feeding, as well as exposure to antibiotics<sup>30 31</sup>. A Cochrane Review in 2020 reported the benefits of ACS in reducing NEC in preterm neonates<sup>20,21,32</sup>. There are concerns that the use of ACS may cause maternal and neonatal sepsis in women with premature membrane rupture<sup>20</sup>, however, there is a benefit seen in lower rates of early neonatal sepsis and this benefit outweighs the risk. However, it is recommended that whenever administering ACS a thorough infection screening is done on the woman. In this comparative, prospective study we did not find a statistical association between increased incidence of neonatal sepsis and ACS exposure. A possible explanation for the observed differences would be that at MNH where the study was carried out, all preterm neonates are given antibiotics.

Our study also reported reduced early neonatal deaths among ACS-exposed preterm neonates. This finding agrees with what is known and adds local evidence that when appropriate use of ACS is done: correct identification of at-risk women, proper estimation of gestation age, complete dose and time from administration to delivery are observed then outcomes are improved.

## Strengths and limitations

Our study had several strengths, this is the first study to assess the use of ACS and preterm birth outcomes in MNH since the National ACS guidelines were introduced in the country in 2015. We ensured women who were exposed received the complete dose at MNH and were followed through. Furthermore, we verified the gestation age of neonates using the New Ballard score done within 24 hours of birth.

The study limitations were that we had a small number of participants and were not able to have a sub-analysis by gestation age, multiple pregnancies or birth weight which would have strengthened the study. This was due to time and budget constraints. We only recruited women who received the completed ACS dose at MNH. Women who were referred from other facilities and delivered at MNH may have received a partial dose before arrival. As a mitigation, we reviewed all maternal medical records and documented all medication given and excluded those with partial ACS exposure.

Almost half of ACS-exposed neonates were delivered by caesarian section. Unfortunately, this was not documented as elective or emergency caesarian section and whether the delivery was induced or spontaneous, which would also explain the completed course of ACS. This study also looked only at ACS and did not document additional interventions such as use of antibiotics or tocolytic therapy to eligible women as recommended by WHO<sup>15</sup>.

### *Implication for practice, research and policy*

Caring for preterm neonates is resource intensive and may require advanced interventions that are not always available in the LMICs. This study highlights the benefits of ACS in a LMIC and reduced RDS potentially reducing need for oxygen therapy and other interventions which can have a great impact in the overall healthcare.

The country's guideline recommends ACS to be administered to women at risk of preterm birth between 28-34 weeks and is silent on the gestation age of 34<sup>+1</sup> - 36<sup>+7</sup> weeks, yet there was a large number of women in this group given ACS.

This study was done at the national hospital where there is the most expertise and trained personnel who also train the next generation of medical practitioners. There is a need to have local context-specific research on the different groups including providers' training and practices, and health benefits of women and their preterm neonates. There is also a need to review the local literature and expertise revise the available guidelines and revisit health workers training to ensure proper administration of ACS among eligible women.

## Conclusion

Antenatal corticosteroid exposure was significantly associated with a reduction of RDS and early neonatal death among preterm neonates. In a country where preterm birth constitutes close to 10% of all deliveries, it is important to ensure proper scaling up of ACS use.

## Conflicting interests

Authors declare no potential conflict of interest concerning the research, authorship and or publication of this article.

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## References

1. Walani. SR. Global burden of preterm birth. *Int J Gynaecol Obstet* 2020;150(1):31-33.
2. World Health Organization. Preterm birth. Fact sheet 2018 [cited 2022 June ]. Available from: <https://www.who.int/news-room/fact-sheets/detail/preterm-birth> accessed June 2022.
3. Liu LD, Oza SM, Hogan DP, Chu YM, Perin JP, Zhu JP, Lawn JEP, Cousens SP, Mathers CP and Black REP. Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. *The Lancet (British edition)* 2016;388(10063):3027-35.
4. Mabrouk A, Abubakar A, Too EK, Chongwo E and Adetifa IM. A Scoping Review of Preterm Births in Sub-Saharan Africa: Burden, Risk Factors and Outcomes. *Int J Environ Res Public Health* 2022;19(17)
5. Chawanpaiboon S, Vogel JP, Moller A-B, Lumbiganon P, Petzold M, Hogan D, Landoulsi S, Jampathong N, Kongwattanakul K, Laopaiboon M, Lewis C, Rattanakankochai S, Teng DN, Thinkhamrop J, Watananirun K, Zhang J, Zhou W and Gülmezoglu AM. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. *Lancet Glob Health* 2019;7(1):e37-e46.
6. Ayebare E, Ntuyo P, Malande OO and Nalwadda G. Maternal, reproductive and obstetric factors associated with preterm births in Mulago Hospital, Kampala, Uganda: a case control study. *Pan Afr Med J* 2018;30:272.
7. Pervin J, Rahman SM, Rahman M, Aktar S and Rahman A. Association between antenatal care visit and preterm birth: a cohort study in rural Bangladesh. *BMJ Open* 2020;10(7):e036699.
8. Jena BH, Biks GA, Gete YK and Gelaye KA. Effects of inter-pregnancy intervals on preterm birth, low birth weight and perinatal deaths in urban South Ethiopia: a prospective cohort study. *Matern Health Neonatol Perinatol* 2022;8(1):3.
9. Alamneh TS, Teshale AB, Worku MG, Tessema ZT, Yeshaw Y, Tesema GA, Liyew AM and Alem AZ. Preterm birth and its associated factors among reproductive aged women in sub-Saharan Africa: evidence from the recent demographic and health surveys of sub-Saharan African countries. *BMC Pregnancy Childbirth* 2021;21(1):770.
10. Blencowe H, Lee ACC, Cousens S, Bahalim A, Narwal R, Zhong N, Chou D, Say L, Modi N, Katz J, Vos T, Marlow N and Lawn JE. Preterm birth-associated neurodevelopmental impairment estimates at regional and global levels for 2010. *Pediatric research* 2013;74 Suppl 1(december):17-34.
11. Alganabi M, Lee C, Bindi E, Li B and Pierro A. Recent advances in understanding necrotizing enterocolitis. *F1000Res* 2019;8
12. Holme N and Chetcuti P. The pathophysiology of respiratory distress syndrome in neonates. *Paediatrics and Child Health* 2012;22(12):507-12.
13. Robertson B. Corticosteroids and surfactant for prevention of neonatal RDS. *Ann Med* 1993;25(3):285-8.
14. Roberts D, Brown J, Medley N and Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation



- for women at risk of preterm birth. *Cochrane Database Syst Rev* 2017;3(3)
15. World Health Organization. WHO recommendation on tocolytic therapy for improving preterm birth outcomes. Geneva World Health Organization.; 2022 [cited 2022 2nd November ]. 98]. Available from: <https://www.who.int/publications/i/item/9789240057227>.
  16. RCOG. Antenatal Corticosteroids to Reduce Neonatal Morbidity and Mortality. *Royal College of Obstetricians and Gynaecologists* 2010(7):3-3.
  17. ACOG. Committee Opinion No. 713 Summary: Antenatal Corticosteroid Therapy for Fetal Maturation. *Obstetrics and gynecology (New York 1953)* 2017;130(2):493-94.
  18. Vogel JP, Souza JP, Gülmezoglu AM, Mori R, Lumbiganon P, Qureshi Z, Carroli G, Laopaiboon M, Fawole B, Ganchimeg T, Zhang J, Torloni MR, Bohren M and Temmerman M. Use of antenatal corticosteroids and tocolytic drugs in preterm births in 29 countries: an analysis of the WHO Multicountry Survey on Maternal and Newborn Health. *The Lancet* 2014;384(9957):1869-77.
  19. Greensides D, Robb-McCord J, Noriega A and Litch JA. Antenatal Corticosteroids for Women at Risk of Imminent Preterm Birth in 7 sub-Saharan African Countries: A Policy and Implementation Landscape Analysis. *Glob Health Sci Pract* 2018;6(4):644-56.
  20. McGoldrick E, Stewart F, Parker R and Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database of Systematic Reviews* 2020(12)
  21. Travers CP, Clark RH, Spitzer AR, Das A, Garite TJ and Carlo WA. Exposure to any antenatal corticosteroids and outcomes in preterm infants by gestational age: prospective cohort study. *BMJ* 2017;356:j1039.
  22. Gulersen M, Gyamfi-Bannerman C, Greenman M, Lenchner E, Rochelson B and Bornstein E. Time interval from late preterm antenatal corticosteroid administration to delivery and the impact on neonatal outcomes. *Am J Obstet Gynecol MFM* 2021;3(5):100426.
  23. Tanzania URo. Administration of Antenatal Corticosteroids in Pre-Term Labour: Tanzania Ministry of Health and Social Welfare, 2015:8-10.
  24. Guruvare S, Basu B, Rai L, Lewis L, Hebbar S and Adiga P. Relationship of time interval between antenatal corticosteroid administrations to delivery with respiratory distress in preterm newborns. *Int J Infertil Fetal Med* 2015;6(3):128-32.
  25. Whitley E, Ball J, Moher D, Dulberg CS, Wells GA, Machin D, Campbell MJ, Fayers P, Pinol A, Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, Peterson E, Tomlanovich M, Altman DG, Altman DG, Gattinoni L, Tognoni G, Pesenti A, Taccone P, Mascheroni D, Labarta V, Malacrida R, Giulio PD, Fumagalli R, Pelosi P, Brazzi L, Latini R, Zijlstra JG, Ligtenberg JJ, Werf TSvd and Slutsky AS. Statistics review 4: sample size calculations. *Critical Care* 2002;6(4):335-35.
  26. Marín Gabriel MA, Martín Moreiras J, Lliteras Fleixas G, Delgado Gallego S, Pallás Alonso CR, de la Cruz Bértolo J and Pérez Estévez E. [Assessment of the new Ballard score to estimate gestational age]. *An Pediatr (Barc)* 2006;64(2):140-5.
  27. Gyamfi-Bannerman C, Thom EA, Blackwell SC, Tita AT, Reddy UM, Saade GR, Rouse DJ, McKenna DS, Clark EA, Thorp MJ, Chien EK, Peaceman AM, Gibbs RS, Swamy GK, Norton ME, Casey BM, Caritis SN, Tolosa JE, Sorokin Y, VanDorsten JP, Jain L and Network NM-FMU. Antenatal Betamethasone for Women at Risk for Late Preterm Delivery. *N Engl J Med* 2016;374(14):1311-20.
  28. Kearsley EOR, Been JV, Souter VL and Stock SJ. The impact of the Antenatal Late Preterm Steroids trial on the administration of antenatal corticosteroids. *Am J Obstet Gynecol* 2022;227(2):280.e1-80.e15.
  29. Karakaya BK, Tasci Y, Yoruk O, Kansu-Celik H and Canpolat FE. Comparing neonatal respiratory morbidity in neonates delivered after 34 weeks of gestation with and without antenatal corticosteroid. *Pakistan journal of medical sciences* 2017;33(6):1390-94.
  30. Bellodas Sanchez J and Kadrofske M. Necrotizing enterocolitis. *Neurogastroenterology and motility* 2019;31(3):e13569.
  31. Isani MA, Delaplain PT, Grishin A and Ford HR. Evolving understanding of neonatal necrotizing enterocolitis. *Curr Opin Pediatr* 2018;30(3):417-23.
  32. Roberts D and Dalziel S. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database Syst Rev* 2006(3).