

Research Article

ISSN 2077-5628

The Effect of Antenatal Corticosteroid for Improving Preterm Outcome At Aljala Maternity and Gynecology Hospital, Neonatal Intensive Care Unit (Tripoli, Libya)

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Received 20 March 2021 / Accepted 16 April 2021

ABSTRACT

Global efforts to reduce neonatal mortality and lifelong disability demand universal action for preterm birth. Antenatal corticosteroid therapy is strongly recommended by WHO to improve preterm birth outcome.

To assess the effect of antenatal corticosteroid (ACS) on the morbidity and mortality in preterm (PT) babies.

This comparative cross-sectional study was conducted by reviewing 252 randomly selected medical records of preterm infants at Aljala Maternity Hospital at Neonatal Intensive Care Unit (NICU) in the period from January 1st, 2016 to December 31st 2017. Major congenital anomalies and extreme preterm newborns were excluded from the study. The preterm gestational age (GA) enrolled in the study was from 29 0/7 to 36 6/7 weeks gestation. The study sample was divided into two groups; preterm babies who received ACS and preterm babies who did not receive ACS. The data analyzed were; sex, gestational age, Mode of Delivery (MOD), Apgar score: 1st and 5th minute, cord ABG, length of stay, prematurity complications, and outcome. Collected data coded and IBM SPSS Statistics software version 22 was used for analysis.

The study sample was divided into two groups 147 (58.3%) of the preterm infants in the ACS group and 105 (41.7%) of the preterm infants in the no-ACS. The percentage of babies with normal Apgar in the 1st min was 73.5% and 63.8% respectively. The study revealed a higher rate of severely low 1 minute Apgar ($P=0.003$) and a higher rate of severe acidosis in the no-ACS ($P=0.019$). Respiratory distress syndrome (RDS) complicated a lower rate 21.1% and it was less severe in preterm babies of the ACS group ($P=0.018$), also a lower rate of Intraventricular Hemorrhage (IVH) in the ACS patients (0.7%) than in the no-ACS group (3.8%). Regarding the length of stay; 8.8% of ACS patients admitted for more than 28 days compared with 14.3% of the no-ACS patients ($P=0.129$). A higher rate of death before discharge 27.6% in the no-ACS group found versus 8.2% in the ACS group ($P=0.001$). The prematurity complication and mortality are less in babies who received ACS. Antenatal corticosteroids should be considered routine for preterm delivery.

Key words- Antenatal; Corticosteroid; Preterm infants; RDS; Aljala.

INTRODUCTION

(SDG) era was launched by the WHO in “Survive and thrive”, Not only decreased the mortality rate in children less than five but also provided a better chance at survival in the sustainable development goal, Ending preventable deaths in neonates to decrease neonatal mortality rate to less than 12 per 1000 live births by 2030 is targeted at SDG3.^{1,2} Prematurity is the leading cause of death in the neonatal period, and its complications account for most of preterm morbidity. The main cause of death in preterm babies is respiratory distress syndrome (RDS), due to lung immaturity and surfactant deficiency.³ RDS and other morbidities as IVH and necrotizing enterocolitis (NEC) are inversely related to preterm gestational age.^{4,7} Late preterm infants are also prone to respiratory disorders.³ Preterm babies are prone to more risk of oxygen therapy and ventilation complications.⁸ Intraventricular hemorrhage (IVH) is a devastating neurological complication that may cause

long-term disability. It is more common in extreme preterm infants with birth weight 500-750 g.⁹ The risk factors for IVH include vaginal delivery, low Apgar score, severe RDS, pneumothorax, hypoxia, hypercapnia, seizures, patent ductus arteriosus, thrombocytopenia, and infection.^{10,11} Most preterm newborns with IVH are asymptomatic and the diagnosis is based on cranial ultrasound screening. Papile classification is based on the location and the extent of IVH is used to determine the severity.¹²

Antenatal steroid treatment for mothers at risk of preterm birth Came to be the most effective intervention for reducing early neonatal mortality and morbidity since it was first described in 1972 by Liggins and Howie.^{13,14} It is now considered standard practice in most countries. Since the NIH Consensus Statement in 1994 there is wide utilization of antenatal steroids in North America and Western Europe.¹⁵ Its use before 34 weeks of pregnancy reduces the rates of major neonatal morbidities, RDS, IVH, and NEC. It also reduces the need for invasive ventilation thus decreasing the



rate of chronic lung damage.¹⁶ late preterm (LPT) infants previously considered as mature as term infants are recently known to be at a higher risk of morbidity and mortality.^{17,18} As late preterm infants represent the majority of premature infants, they have a considerable impact on the healthcare system compared with full-term infants.¹⁹⁻²³ There is still controversy about the ACS beneficial effects extending beyond the 34th week. The current study aimed to assess the effect of antenatal corticosteroids on the outcome of preterm babies by comparing the morbidity and mortality of preterm babies who received ACS and those who did not receive ACS.

MATERIALS AND METHODS

This comparative cross-sectional study was conducted by reviewing 252 randomly selected medical records of preterm infants at Aljala Maternity Hospital NICU in the period from January 1st, 2016 to December 31st, 2017. Aljala Maternity Hospital is a governmental specialized tertiary university hospital that provides maternity and level III NICU services in Tripoli, in addition to a high percentage of referrals of high-risk pregnancies from other external hospitals and clinics. Major congenital anomalies and extreme preterm newborns were excluded from the study. The preterms GA enrolled in the study was from 29 0/7 to 36 6/7 weeks gestation. The study sample was divided into two groups; preterm babies who received ACS (147) and preterm babies who did not receive ACS (105). The information analyzed w; sex, gestational age, MOD, Apgar score: 1st and 5th minute, cord arterial blood gas (ABG), length of stay, and outcome. Complications of prematurity were studied as RDS, NEC, and IVH. GA is divided into 3; very premature: 29 0/7 to 31 6/7 and moderate premature: 32 0/7 to 33 6/7 and late premature 34 0/7 to 36 6/7. RDS confirmed by chest X-ray findings and O2 requirements, NEC was diagnosed by clinical examination and abdominal X-ray, and IVH was diagnosed by head ultrasonography. Collected data was coded and statistically analyzed using IBM SPSS Statistics software version 22 was used for analysis, frequency, percentage, mean and standard deviation used to describe the data, chi-square used to find the significance of the differences between categorical variables and t-test for independent groups used for the difference between means, a P value of less than 0.05 is considered significant.

RESULTS

The main concern in the current study was the influence of antenatal corticosteroids on the outcome of premature babies. In the study period, 20735 alive babies were born at Aljala maternity hospital. 25.9% of them (5365) were admitted to NIC for different causes, 252 medical records of premature babies with GA between 29 and 36 complete weeks of gestation were reviewed. Among the study sample, 147(58.3%) pregnancies that received ACS were identified, the remainder of pregnancies did not receive ACS.

The basic maternal and neonatal characteristics showed no significant difference between the two groups (sex, GA, MOD, maternal age, and maternal diseases) (Table 1).

Table 1: Demographic and obstetric characteristics of study sample

Variable	Antenatal corticosteroids (n=147) N (58.3%)	No antenatal corticosteroids (n=105) N (41.7%)	P value
Sex			
Male	76(51.7%)	55(50.9%)	0.899
Female	71(48.3%)	49(46.7%)	
GA			
30 <32	40(27.2%)	28(26.7%)	0.129
32 <34	57(38.8%)	29 (27.6%)	
34<37	50(34%)	47(44.8%)	
MOD			
Vaginal	58(57.8%)	49(45.5%)	0.519
EM C/S	5 (3.4%)	3(50.5%)	
EL C/S	84(32.7%)	52(4.0%)	
Maternal age	33.1 ±6.7	32.5 ±6.3	0.515
Maternal Disease			
No illness	95(64.6%)	79(75.2%)	0.078
DM	13(8.8%)	11(10.5%)	
HTN	18(12.2%)	3(2.9%)	
DM& HTN	8(5.4%)	2(1.9%)	
Chorioamnionitis	2(1.4%)	0(0%)	
PROM	5(3.4%)	3(2.9%)	
Abruption	2(1.4%)	3(2.9%)	
Other illness	4(2.7%)	4(3.8%)	



Among the 252 PT newborns assessed for short-term outcomes, most of the babies in the ACS group and the no-ACS group had normal Apgar in 1st min (73.5% and 63.8% respectively). The no-ACS group had a higher rate of severely low 1 minute Apgar that was statistically significant ($P=0.003$), and a higher rate of moderately low 5-minute Apgar in the no-ACS (10.5%), which was also statistically significant ($P=0.030$). Cord ABG was done only for 179 infants and showed severe acidosis in 17.4% of neonates with no-ACS compared with 5.5% in the ACS group ($P=0.019$). A higher rate of infants had no complications in the ACS group 76.9% compared with the no-ACS 57.1%. RDS complicated 21.1% of the ACS group and 36.2% of the other group, one patient 0.7% of infants in the ACS group had IVH while 3.8% of infants in the no-ACS group had IVH. NEC rate was higher in the ACS at 1.4% than in the no-ACS 1%, these results were statistically significant ($P=0.013$).

RDS rate was recognized as more common than other causes of morbidity and mortality in premature babies. Analyzing RDS severity, at a lower rate of severe cases in the ACS group (19.4%) compared to the no-ACS group (52.6%), that was statistically significant ($P=0.018$).

Studying the distribution of the developing complication according to GA, the very premature infants with ACS had 44% with no complication, but all infants in the no-ACS group had complications. A lower rate of RDS in the very preterm ACS group than in the no-ACS group (51% and 85%), and a lower rate of IVH in the ACS group than in the other group (2.4% and 14.4%), but a higher rate of NEC in the ACS than in the no-ACS (2.4% and 0%) which was statistically significant ($P=0.001$). In the moderate premature the ACS group had a higher rate of infants without complication (84% and 62%), a lower rate of infants with RDS (14% and 31%), a lower rate of infants with NEC (1.8% and 3.5%) and no infants had IVH compared to the no-ACS (0% and 3.5%). Most of the infants in the late premature had no complications in the ACS and the no-ACS (96% and 91.3%). A lower rate of RDS in the late preterm ACS group (4%) compared with the rate in the no-ACS group (8.7%). No late preterm infants had IVH or NEC in both groups, but these results were not statistically significant ($P>0.05$).

Observing the length of stay in the study sample, 14.3% of the no-ACS patients admitted for more than 28 days compared with 8.8% of the ACS patients ($P=0.129$). 27.6% of the no-ACS group who passed away before discharge versus 8.2% of the ACS group ($P=0.001$).

Table 2: Neonatal morbidity and short-term outcome at NICU in Aljala Hospital

Variable	ACS (n=147)	NO-ACS (n=105)	P value
<i>Apgar 1</i>			
7-10	108(73.5%)	67(63.8%)	0.003
4-6	29(19.7%)	15(14.3%)	
0-3	7(4.8%)	20(19%)	
Not attended	3(2.0%)	3(2.9%)	
<i>Apgar 5</i>			
7-10	139(94.6%)	88(83.8%)	0.030
4-6	4(2.7%)	11(10.5%)	
0-3	1(0.7%)	3(2.9%)	
Not attended	3(2.0%)	3(2.9%)	
<i>Acidosis</i>			
Normal	58(77.3%)	47(68.1%)	0.019
Mild (PH 7.1-7.2)	19(17.2%)	10(14.5%)	
Sever (PH <7.00)	6(5.5%)	12(17.4%)	
<i>Complication</i>			
RDS	31(21.1%)	38(36.2%)	0.013
NEC	2(1.4%)	1(1%)	
IVH	1(0.7%)	4(3.8%)	
No complication	113(76.9%)	61(57.1%)	
<i>LOS</i>			
1day	17(11.6%)	8(7.6%)	0.129
2-7days	59(40.1%)	52(49.5%)	
8-28 days	58(39.5%)	30(28.6%)	
>28 days	13(8.8%)	15(14.3%)	
<i>Outcome</i>			
No complication	113(76.9%)	61(57.1%)	0.001
Complication and improve	22(15%)	15(14.3%)	
Death before discharge	12(8.2%)	29(27.6%)	



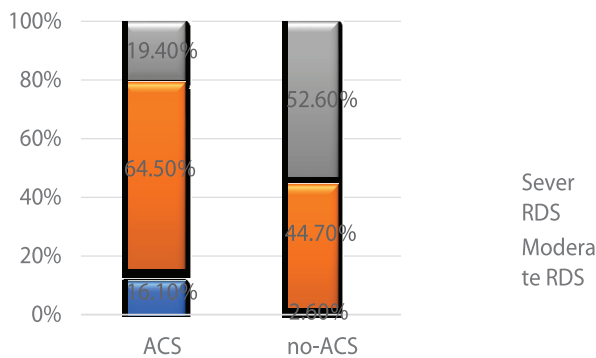


Figure 1: Distribution of RDS severity according to ACS therapy in the study group

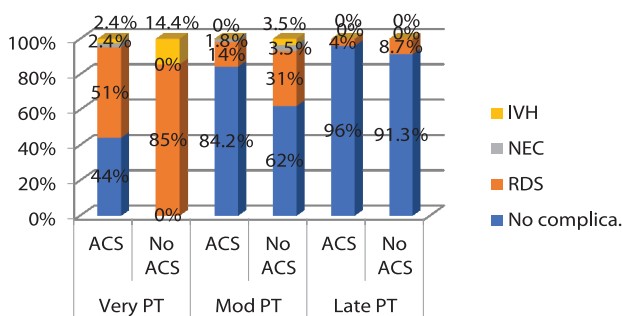


Figure 2: Distribution of complications in relation to GA in the study groups

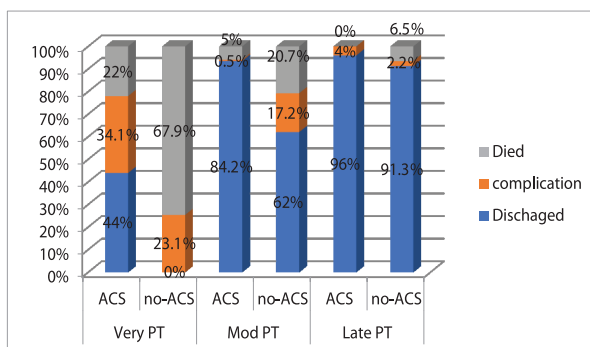


Figure 3: Distribution of outcomes in relation to GA in the study groups

DISCUSSION

Antenatal corticosteroid therapy is aimed at improving newborn outcomes and is strongly recommended by WHO. It is an important maternal intervention step for improving neonatal morbidity and mortality.²⁴ Studying the demographic neonatal and obstetric characteristics shows no significant difference between the preterm group received ACS and the preterm group with no-ACS in gender, GA distribution, maternal diseases, and MOD. Although in both groups vaginal birth was dominating, the rate of elective C/S was higher in the ACS group (32.7%) compared to the no-ACS group (4%).

Analyzing the early effect of corticosteroids at birth, the percentage of babies with normal Apgar in the 1st min was 73.5% and 63.8% respectively. The no-ACS group

had a statistically significant higher rate of severely low 1st minute Apgar (19.7%) indicating that more babies required resuscitation ($P=0.003$), and a higher rate of moderately low 5 minutes Apgar in the no-ACS (10.5%) which was significant statistically ($P=0.030$). This was opposite to Woo Jeng Kim, et al study which emphasized that there was no statistically significant difference between the two groups²⁵ but similar to Kadioglu Simsek et al, the Turkish study results reported that a smaller number of babies required resuscitation and higher Apgar score at 5 minutes in the ACS group²⁶

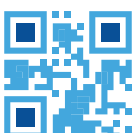
Cord ABG was done only for 179 infants. PH in the withdrawn blood samples showed severe acidosis in the no-ACS group 17.4% compared to 5.5% in the ACS group ($P=0.019$), contrary to the finding of Kadioglu Simsek et al. study where similar pH in the two groups was observed.²⁶

Preventing premature morbidity is a challenge for all NICUs. (76.9%, and 57.1%) of the premature babies had no complications during admission in the ACS group and the no-ACS group, respectively which was statistically significant ($P=0.013$). RDS in premature newborns is a common cause of morbidity and mortality. Evaluating RDS in the two study groups, the RDS rate was lower in the ACS group (21%) and (36.2%) than in the no-ACS group. Similar to Y.-C. Wang et al study reported a decrease in the incidence of RDS in premature infants who received ACS.²⁷ Not only the rate but also the severity of RDS was less in the ACS group (19.4%) compared to the no-ACS group (52.6%), which was statistically significant ($P=0.018$). this was also the result of E. Bancalari, Matthew's study.²⁸

The main neurological disease that affects preterm is intraventricular hemorrhage. The rate of IVH was lower in the ACS group (0.7%) than in the no-ACS group (3.8%). This was further analyzed according to the GA, and the result was that the very premature ACS group had a statistically significant decrease in IVH rate than in the other study group (2.4% versus 14.4% with $P=0.001$) this was also revealed in the moderate premature 1.8% to 3.5% but it was not statistically significant $P=0.100$). Julia C. Wei et al study showed no significant differences in premature > 30 weeks in IVH rate whether received ACS or not.²⁹ Roberts D et al study has shown that antenatal steroids therapy was associated with a decrease in the risk of IVH in neonates born between 29-34 weeks gestational age.¹³

Further evaluation of the complication according to the GA, the very PT ACS group had a lower rate of RDS and IVH. A higher rate of very preterm in the ACS group had no complication compared to the no- ACS which was statistically significant ($P=0.001$), but in the Mod and late preterm, it was statistically not significant. M K Ramadan's study emphasized that ACS administration to mothers for late preterm does not decrease morbidities.³⁰

A lower rate of death before discharge was observed in the ACS patients (8.2%), wherein the no-ACS group the death rate was (27.6%) which was statistically significant ($P=0.001$), despite that the number of very and mod-premature babies were more in the ACS group. This



result was similar to Colm. P Travers et al study revealed a lower rate of death in preterm received ACS compared with infants without ACS exposure.³¹

Further, evaluating the outcome and the GA, the study revealed a significant difference between the study groups. The rate of the very PT and the Mod premature babies was lower in developing complication and death in the ACS infants compared to the No-ACS group that was statistically significant ($P=0.001$ and $P=0.040$) respectively. This difference between the two groups was not statistically significant in the LPT babies. The Vijaya Ontela et al study concluded that there is noticeable effect of the ACS in improving morbidity of the late preterm.³²

CONCLUSION

A better transition of the premature babies at birth with antenatal corticosteroid exposure (ACS). It reduces the need for resuscitation. premature baby complications and mortality are less in babies who received ACS. ACS has not affect in reducing complications in Late premature babies.

RECOMMENDATIONS

Antenatal corticosteroids should be considered routine for preterm delivery. Follow-up studies into childhood are needed for possible harmful effects of antenatal corticosteroids.

ACKNOWLEDGEMENT

Our sincere gratitude and acknowledgment to all Aljala NICU staff members with special thanks to all members who participated in data collection in this study. Special thanks to Mohamed Ben Othman for his valuable help.

REFERENCES

1. Blencowe H, Cousens S, Chou D, Oestergaard M, Say L, Moller AB, Kinney M and Lawn J (2013) Born Too Soon Preterm Birth Action Group. Born too soon: the global epidemiology of 15 million preterm births, *Reprod Health* **10**(1), S2.
2. Pia Britto (2018) UNICEF, New York, USA, Vivienne Chai; Survive and thrive: transforming care for every small and sick newborn. Geneva: World Health Organization; 2018 (WHO/FWC/MCA/18.11).
3. Avery ME and Mead J (1959) Surface properties in relation to atelectasis and hyaline membrane disease, *Am J Dis Child*, **97**, 517-523.
4. Whitsett JA, Pryhuber GS, Rice WR, Warner BB, Wert SE, Avery GB, Fletcher MA and MacDonald MG (1994) Acute respiratory disorders, Neonatology: Pathophysiology and Management of the Newborn, 4th Philadelphia J.B. Lippincott Company, p. 429-452.
5. Hjalmarson O (1981) Epidemiology and classification of acute neonatal respiratory disorders. A prospective study, *Acta Paediatr Scand*. **70**, 773-783.
6. Farrell PM and Avery ME (1975) Hyaline membrane disease, *Am Rev Respir Dis*. **111**, 657-685,
7. Clare M. Rees, Simon Eaton and Agostino Pierro (2009) National prospective surveillance study of necrotizing enterocolitis in neonatal intensive care units, *Journal of Pediatric Surgery* **10**, 1016.
8. W Tin and S Gupta (2007) Optimum oxygen therapy in preterm babies, *Arch Dis Child Fetal Neonatal Ed*. **92**(2), F143-F147.
9. Wilson-Costello D, Friedman H, Minich N, Fanaroff AA and Hack M (2005) Improved survival rates with increased neurodevelopmental disability for extremely low birth weight infants in the 1990s, *Pediatrics* **115**, 997-1003.
10. Antoniuk S and da Silva RV (2000) Periventricular and intraventricular hemorrhage in the premature infants, *Rev Neurol*. **31**, 238-243.
11. Ballabh P (2005) Intraventricular hemorrhage in premature infants: mechanism of disease. *Pediatr Res*. **67**, 1-8.
12. Papile LA, Burstein J, Burstein R and Koffler H (1978) Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm, *J Pediatr*. **92**, 529-534.
13. Roberts D and Dalziel S (2008) Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth, *Cochrane Database Syst Rev*. **3**, CD004454.
14. Liggins GC and Howie RN (1972) A controlled trial of antepartum glucocorticoid treatment for prevention of the respiratory distress syndrome in premature infants, *Pediatrics* **50**, 515-525.
15. National Institutes of Health (1994) Effect of corticosteroids for fetal maturation on perinatal outcomes, *NIH Consensus Statement* **12**, 1-24.
16. Suguihara C and Lessa AC (2005) Strategies to minimize lung injury in extremely low birth weight infants, *J Pediatr*. **81**(1).
17. Wang ML, Dorer DJ, Fleming MP and Catlin EA (2004) Clinical outcomes of near-term infants, *Pediatrics* **114**, 372-376.
18. Tomashek KM, Shapiro-Mendoza CK, Weiss J, Kotelchuck M, Barfield W, Evans S, et al. (2006) Early discharge among late preterm and term newborns and risk of neonatal morbidity, *Semin Perinatol*. **30**, 61-68.
19. Davidoff MJ, Dias T, Damus K, Russell R, Bettgowda VR, Dolan S, et al. (2006) Changes in the gestational age distribution among US singleton births: impact on rates of late preterm birth, 1992 to 2002, *Semin Perinatol*. **30**, 8-15.
20. Santos IS, Matijasevich A, Domingues MR, Barros AJ, Victora CG and Barros FC (2009) Late preterm birth is a risk factor for growth faltering in early childhood: a cohort study, *BMC Pediatr* **9**, 71.
21. Fuchs K, Wapner R (2006) Elective cesarean section and induction and their impact on late preterm births, *Clin Perinatol*. **33**, 793-801.
22. Bird TM, Bronstein JM, Hall RW, Lowery CL, Nugent R and Mays GP (2010) Late preterm infants: birth outcomes and health care utilization in the first year, *Pediatrics* **126**, e311-9.
23. Sreenivas Karnati, Swapna Kollikonda and Jalal Abu-Shaweesh (2020) Late preterm infants -Changing trends and continuing challenges, *Int J Pediatr Adolesc Med*. **7**(1), 36-44.
24. World Health Organization (2015) WHO Recommendations on Interventions to Improve Preterm Birth Outcomes. Geneva,



Switzerland: WHO Press.

25. Woo Jeng Kim, et al. (2018) Antenatal steroid in SGA, *ObstetGynecolSci.* **61**(1), 7-13.

26. Kadioglu Simsek et al. (2019) The Effects of Antenatal Steroid Treatment on Preterm Infants' Early Laboratory Analysis / doi: 10.14744/SEMB.68916

27. Y.-C. Wang et al (2012) Effects of Antenatal Corticosteroids on Neonatal Outcomes in Very-Low-Birth-Weight Preterm Newborns: A 10-Year Retrospective Study in a Medical Center, *Pediatrics and Neonatology* **53**, 178e183.

28. Eduardo Bancalari and Matthew M. Laughon (2019) The Newborn Lung (Third Edition), 2019, chapter 6.

29. Julia C. Wei et al (2016) Impact of Antenatal Steroids on Intraventricular Hemorrhage in Very Low Birth Weight Infants, *J Perinatol.* 2016 **36**(5), 352-356.

30. M K Ramadan and G Hussein (2016) Antenatal corticosteroids in the late preterm period: A prospective cohort study, *J Neonatal Perinatal Med.* **9**(1), 15-22.

31. Colm P Travers et al. (2017) Exposure to any antenatal corticosteroids and outcomes in preterm infants by gestational age, *BMJ* **356**, j1039

32. Vijaya Ontela, Gowri Dorairajan, Vishnu B. Bhat, and Palanivel Chinnakali (2018) Effect of Antenatal Steroids on Respiratory Morbidity of Late Preterm Newborns, *Journal of Tropical Pediatrics* **64**, 531.

