The interaction of maternal obesity and administered betamethasone in the development of fetal respiratory distress syndrome

Keywords
obesity, preterm birth, respiratory distress syndrome, antenatal corticosteroid

Abstract
Introduction
The current study evaluated the effect of obesity on neonatal respiratory distress syndrome (RDS) in pregnant women who were administered ACSs due to the risk of preterm birth and delivered before 34 weeks of gestation.

Material and methods
In this retrospective study, 414 pregnant women who had a singleton pregnancy, were aged 18–40 years, and received two doses of ACS 24 h apart administered between 23+0/7 and 33+5/7 gestation weeks due to the risk of a preterm birth were included. For maximum fetal effect, those who completed the 48-hour steroid treatment and delivered before 34 weeks of gestation were divided into three groups according to BMI at ACS administration.

Results
Gestational age at ACS administration and gestational age at delivery were similar among groups.. Neonatal RDS occurred in 17 (18.6%) newborns in the normal weight group, 40 (17.1%) newborns in the overweight group, and 23 (25.5%) newborns in the obese group. After adjusting for independent effects from maternal age, gestational age at ACS administration, gestational age at delivery, emergency cesarean delivery, fetal birth weight, and fetal gender, we found that RDS rates were significantly higher in the obese group.

Conclusions
Our results suggest that maternal obesity reduces the effects of ACS and that RDS rates are higher in neonates born before 34 weeks of gestation to obese mothers to whom ACS has been administered.Therefore, pregnant women who have a high BMI and who are at risk of preterm birth are more likely to require an adjustment in ACS dosing.

The interaction of maternal obesity and administered betamethasone in the development of fetal respiratory distress syndrome.

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Running Head: Obesity effectson the effects of ACS.

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Abstract

Objective: Obesity is related with an inadequate tissue perfusion and a alteration in drug clearance. It is not clear whether obese women at risk of preterm birth require higher doses of ACSs to optimize the benefits for their preterm infants. In the current study we aimed to evaluate the effect of obesity on neonatal respiratory distress syndrome (RDS) in pregnant women who were administered antenatal corticosteroid (ACS) due to the risk of preterm birth and delivered before 34 weeks of gestation.

Study Design: In this retrospective study 414 pregnant women who had singleton pregnancy, aged between 18–40 years, two dose 24h apart ACS adminstirated between 23+0/7- 33+5/7 gestation weeks due to preterm birth risk, for maximum fetal effect, those who have completed a 48-hour steroid period and delivered before 34 weeks of gestation were devided into three group acording to BMI at ACS administration; (1) control, BMI <25 kg/m2 (n:91); (2) BMI 25-29,9 kg/m2 (n:233); and (3) BMI ≥ 30 kg/m2 (n:90). The primer outcome of the study was defined as presence of neonatal RDS.

Results: Gestational age at ACS administration and gestational age at delivery were similar among groups. Emergency caesarean delivery rates, fetal birth weight, fetal birth weight percentile, rates of male births, 5 min Apgar score, and length of stay in the neonatal intensive care unit (NICU) were similar among the groups. Neonatal RDS was defined 17 (%18.6) newborns in normal weight group, 40 (%17.1) newborns in overweight group and 23 (%25.5) newborns in obese group. After adjusted for independent effects of many variables (maternal age, gestational age at ACS administration, gestational age at delivery, emergency caesarean delivery, fetal birth weight and fetal gender) we found that RDS rates was significantly higher in the obese group.

Conclusion: Our results suggest that maternal obesity reduces the effects of ACS and that RDS rates are higher in neonates born before 34 weeks of gestation to obese mothers to whom ACS has been administered. Therefore, pregnant women who have higher BMI and who are at risk of preterm birth would be more likely to require an adjustment in ACS dosing.

Keywords: Obesity, Preterm birth, Antenatal corticosteroid, Respiratory distress syndrome

Introduction

Obesity is a major health problem worldwide, and its prevalence is especially increasingamong pregnant women. It is known that being overweight or obese during pregnancy isassociated with preeclampsia, gestational diabetes, preterm birth, and other adverse perinataloutcomes [1]. Today, premature deliveries continues to challenge obstetricians that is one of theleading causes of neonatal morbidity and the most common reason for hospitalizations duringthe antenatal period [2]. In the presence of preterm birth risk, antenatal corticosteroid (ACS)administration accelerates fetal lung development, thus reducing neonatal mortality andmorbidity [3]. Guidelines have recommended 24 mg dexamethasone or 12 mg betamethasone divided over a 24-h period for any at-risk pregnancies regardless of maternal height and weight **between $23+^{0/7}$ and $34+^{0/7}$ gestational weeks [4].**

Obesity is related with an inadequate tissue perfusion and a alteration in drug clearance [5]. It is not clear whether obese women at risk of preterm birth require higher doses of ACSsto optimize the benefits for their preterm infants [6] and the literature has little data about therole of maternal body mass index (BMI) on the efficacy of ACS [7, 8, 9, 10, 11]. Hashima etal. [11] have reported that after ACS administration, there is no relationship between maternal

BMI and adverse neonatal outcomes. Another study has reported this same observation, although a post hoc analysis found an increased probability of bronchopulmonary dysplasia, and brain injury and fetal death in infants born to pregnant with a BMI ≥ 40 kg/m2 [10]. Studies on pharmacokinetics have declared that pregnant women with increased BMI may requirehigher doses of ACSs because of the larger volume of distribution [9]. The aim of the currentstudy was to evaluate the role of maternal BMI on RDS in pregnant women who wereadministered ACSs because of the risk of preterm birth and who delivered at ≤ 34 gestational weeks.

Materials and Methods

Study population

The study involves pregnant women with a singleton pregnancy who were between 18 and 40years old who were given two doses 24h apart of ACS between $23+^{0/7}$ and $33+^{5/7}$ gestational weeks because of the risk of preterm birth and for maximum fetal effect. Those who completed the 48-h steroid period of administration and delivered at ≤ 34 gestational weeks were followed up at our clinic between May 2018 and August 2022. Hence we record and compare all interval times between administration of steroids and delivery in each group

of patients. These patientswere divided into three groups based on their BMIs as follows: normal body size group (control; BMI <25 kg/m2), overweight group (BMI = 25–29.9 kg/m2), or obese group (BMI ≥30 kg/m2). Of the 610 pregnant women evaluated, 196 were excluded for the followingreasons: 1) multiple pregnancy, 2) congenital or chromosomal abnormalities, 3) presence oftype 1 or 2 diabetes and gestational diabetes mellitus, 4) chronic/gestational hypertension andpreeclampsia, 5) fetal growth restriction, 6) abnormal umbilical artery Doppler flows, 7) premature preterm rupture of membranes, 8) systemic chronic disease, 9) smoking or alcoholuse, 10) cases having missing data, 11) presence of neonatal sepsis and 12) presence of fetalmetabolic acidosis because of its relationship between neonatal tachypnea. Finally, studyinvolves 414 pregnant women who delivered at Kayseri City Hospital. Figure 1 provides theflow chart of the steps used for determining the study population.

Primary outcomes and definitions

The primary outcome of the current study was defined as presence of neonatal respiratorydistress syndrome (RDS). The gestational age was determined using the date of the beginningof the patient's last menstrual period, if known. For the pregnant women who did not knowthe last menstrual period, the gestational week was determined and confirmed by using thefirst trimester crown-rump length measurement. The protocol was to administer two intramuscular doses of 12 mg ACS 24 h apart [4]. As a routine practice of our clinic, Betamethasone Acetate + Betamethasone Disodium Phosphate (CELESTONE CHRONODOSE 1 ml 1 ampoule) (Schering Plough) was preferred in antenatal corticosteroid administration to all includedpregnant women. ACS was applied between 23^{+0} and 33^{+6} gestational weeks acording to guideline [4]. The diagnosis of fetal growth restriction is made according to Delphiconsensus criteria [12, 13]. Neonatal RDS was defined by the pediatrician. After excludedother causes of RDS, the presence of diffuse, fine granular densities and decreased lungcapacity with increased oxygen requirement (fractional concentration of inspired oxygen>0.4) were used to diagnose RDS [14].

Ethical statement

This retrospective cohort study was conducted at Kayseri City Hospital Obstetric Clinics, Turkey. Ethics Committee of Kayseri City Hospital (decision number: 520) was approved the study and conducted according to the Helsinki Declaration.

Statistical analyses

We defined the number of our study groups according to study entitled with 'The effect of maternal body mass index on neonatal outcome in women receiving a singlecourse of antenatal corticosteroids' [11], which was accepted in a respected journal in theliterature, in

order to avoid insufficient number of patients in our study, not to affect ourresults, and especially to avoid type 2 errors. Statistical analyses were conducted using SPSSver. 21 (IBM Corp., Armonk, NY, USA). The normality of the data was obtained withKruskal–Wallis H test, and assumption of variance homogeneity was obtained with theLevene test. The data are presented as the mean ± standard deviation, median ($25_{th}$$75_{th}$percentile), or n (%); P <0.05 was considered statistically significant. One-way ANOVAanalysis of variance was conducted to compare multiple groups (Tukey's *post-hoc* test) afterevaluating for normal distribution. Categorical data in paired groups were compared using thechi-squared test; non-categorical data in paired groups were compared using the Mann–Whitney U test. The difference among the groups was considered statistically significantwhen p <0.05. One-way analysis of covariance (ANCOVA) was also applied to compare thedifferences of variables between groups by adjusting the maternal age, gestational age at ACSadministration, gestational age at delivery, emergency caesarean delivery, fetal birth weightand fetal gender.

Results

Table 1 provides the demographic characteristics of the patients. Maternal age, BMI at ACSadministration, and parity were significantly higher in obese group compared to normal andoverweight group. Ethnicity and previous caesarean delivery delivery rates were similaramong the three groups.

Table 2 provides the perinatal outcomes and neonatal RDS rates among the groups. Gestational age at ACS administration was 30 (28-31) weeks in normal weight group, 30 (29-31) weeks in overweight group and 31 (30-31) weeks in obese group and gestational age atACS administration was similar among the groups (p= 0.494). Gestational age at delivery was 32 (31-32) weeks in normal weight group, 32 (31-33) weeks in overweight group and 32 (32-33) weeks in obese group and gestational age at delivery was similar among the groups (p=0.642). Interval between administration of ACS and delivery were similar among groups (p=0.820). Emergency caesarean delivery rates, fetal birth weight, fetal birth weightpercentile, rates of male births, 5 min Apgar score, and length of stay in the neonatal intensivecare unit (NICU) were similar among the groups (p= 0.560, p= 0.150, p= 0.820, p= 0.612, p=0.960, and p= 0.790, respectively). Neonatal RDS was observed in 17 (18.6%) newborns inthe in normal weight group, 40 (17.1%) in overweight group, and 23 (25.5%) in the obesegroup. After adjusted with bonferroni test to compare the important multiple variables amonggroups (maternal age, gestational age at ACS administration, gestational age at delivery, emergency caesarean delivery, fetal weight and male fetal gender) we found that RDS rateswas significantly higher in the obese group compare to normal and overweight group (p=0.032).

Discussion

The goal of the current study was to evaluate the effect of obesity on neonatal RDS inpregnant women who were administered ACS because of the risk of preterm birth and whodelivered at ≤34 gestational weeks. The most important difference of the study, whichdistinguishes it from other studies in the literature, is the evaluation of the fetuses that wereadministered steroids and were born before 34 weeks of gestation. The importance of this isthat the incidence of RDS after 34 weeks of gestation decreases significantly which is theprimary result of the study. After adjusted independent variables the key finding of the studywas that maternal obesity reduces the effects of ACS and that neonatal RDS rates were higherin the obese group whom administered ACS especially fetuses delivered before 34 weeks ofgestation.

Results in thecontext of previous studies on maternal obesity and most animal studies on ACS were based maternal dosing

The literature has limited studies that have evaluated this phenomenon. In these studies, thepresence of different inclusion and exclusion criteria, the absence of multiple logisticregression analyses for important cofounders, the variable patient subgroups, and fetusesdelivered at term made it difficult to assess the effect of obesity on premature delivery related toadverse perinatal outcomes. In a study to Hofer et al. [7], patients given ACS for the risk ofprematurine delivery at <34 gestational weeks were divided into normal weight, overweight, and obesegroups. They reported that there were no ststisticlly differences among all groups for othermorbidities, such as mechanical ventilation, bronchopulmonary dysplasia and perinatal death [7]. In this study authors included patients with antepartum hemorrhage, preterm prelaborrupture of membranes, pre-eclampsia, and other complications. More importantly, thegestational age at delivery was ~35 weeks in all three groups. In another retrospective study, no relationship was obtained between maternal BMI and adverse neonatal outcomes afterACS administration, although the fetuses born at <34 gestational weeks were analyzed in thethat study for only the patients with BMI < 25 or ≥ 25 kg/m2, which limited the study's abilityto demonstrate a BMI effect. [10]. Hashima et al. [11] have found no association amongmaternal BMI, exposure to ACS, and neonatal outcomes after corticosteroids were given topatients at risk of preterm birth. That study was found to be under powered with a risk ofselection bias because of differing rates of birth within one week of ACS administration towomen with a normal BMI [11]. The most important limitation of that study was the inclusionof women who had received only a single course of ACSs and who were classified as BMI<25 or ≥25 kg/m2 and fetuses born in late preterm and term

pregnancy. In a well-designedretrospective cohort study of 535 women that included admission to the NICU, deliveries at<34 gestational weeks, and hospitalization before delivery, the primary outcome assessed wasthe presence of RDS. Although increased ACS doses were related with less pulmonarysurfactant doses, no association was reported between neonatal RDS incidence and maternalBMI; however, the study did not track other neonatal health outcomes [15]. On the otherhand, in their prospective pharmacokinetic study, Della Torre et al. [9] has found thatpregnant with a higher BMI may require higher doses of ACS because of the larger volume ofdistribution. Vricella et al. [16] have reported that blood volume rises with adiposity; for thisreason, it is expected that the volume of distribution for ACS dosing alter with increasing BMI [16]. In addition, most animal studies on ACS based maternal dosing on weight [17, 18]. In a amimal study Schmidt AF et al. [18] they report the pharmacokinetics and pharmacodynamics of oral dosing of ACS using a preterm sheep model. They found that oraldexamethasone-phosphate (Dex-P) had lower bioavailability than oral betamethasone-phosphate (Beta-P), giving a lower maximum maternal and fetal concentration. A single oral dose of 0.33 mg/kg of Beta-P was equivalent to the standard clinical treatment assessed at 2 days; 2 doses of 0.16 mg/kg of oral Beta-P were equivalent to the standard clinical treatment at 7 days as assessed by lung mechanics and gas exchange after preterm delivery and ventilation. In contrast, oral Dex-P was ineffective because of its decreased bioavailability [18].

Strengths and Limitations

The important strengths of the present study were the large sample size of 414 women andthat all women entered the study at <34 gestational weeks, which enabled us to assess thelikelihood of neonatal RDS at lower gestation periods. Strength of the study was theavailability of the datas from a reference center where experienced obstetricians andneonatologists had managed all pregnancies and newborns. Because of our large sample size, we were able to divide our study population into three relevant BMI categories, whichdiffered from that of previous studies. We were then able to observe the differences amongwomen with different BMIs, and more specifically, differences between those at the upperBMI extremes. The other important strength was the presence of datas aboutthe interval between administration of ACS and delivery in each group of patients is extremely important because the risk of RDS is the lowest when baby is delivered during 48-72 hours after administration, and not alter than 7 days, after this time the risk may even increase again. Considering our study group, approximately 334 (80.6%) of 414 patients deliveried between 2-7 days after ACS was applied when the effectiveness of ACS was maximum. This ratio and

the careful selection of the patients to whom ACS will be applied have enabled us to more clearly show the preventive effect of ACS on RDS. In literature it is well documented thata longer ACS delivery interval is associated with a higher risk of RDS in both single and twin pregnancies [19, 20]. There were several limitations to the current study. First of all this was aretrospective design. Second, only three pregnant women in our study population had a BMI>35, which made a difference in evaluating the effects of moderate and morbid obesity on theeffects of ACS and presence of RDS. Third limitation was the the heterogeneity among cesarean delivery indications. **In another important limitation is complexity of obesity during pregnancy, such as presence of hyperlipidemia or hypercholesterolemia. Does this affect the effectiveness of ACS or neonatal RDS? Is obesity a root cause or mediator? In a routine study practice in Kayseri City Hospital, measurement of maternal HDL, LDL, total cholesterol or other apoproteins and lipoproteins is not performed during pregnancy. Adding and evaluating these parameters will certainly contribute greatly to the study, but the retrospective design of our study causes us to reach these results.** Finally, the effect of obesity would much clearer ifstudies are conducted on a larger population and that evaluate the effect of ACSpharmacokinetically in addition to clinical neonatal findings.

Conclusion

Our results suggest that maternal obesity reduces the effects of ACS and that RDS rates are higher in neonates born before 34 weeks of gestation to obese mothers to whom ACS has been administered. Therefore, pregnant women who have higher BMI and who are at risk of preterm birth would be more likely to require an adjustment in ACS dosing.

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Author Contributions

Mehmet Ak, Mefkure Eraslan Sahin, Erdem Sahin: Study design, manuscript writing, final editing andfinal approve of the study.

Yusuf Madendag, Cevat Rifat Cundubey, Mehmet Ak, and Ilknur Col Madendag: Data analyzing, preparing, analyzing data and manuscript writing

Osman Bastug: Definition of RDS and management of fetuses

All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Conflict of Interest Statement

Authors have stated no conflict of interest.

Informed Consent

Informed consent was obtained from all individuals included in this study.

Ethical Approval

This retrospective cohort study was conducted at Kayseri City Hospital Obstetric Clinics, Turkey. Ethics Committee of Kayseri City Hospital (decision number: 520) was approved the study and conducted according to the Helsinki Declaration." "Ethical Approval. The local Institutional Review Board deemed the study exempt from review." The contents within these two titles need to be consistent, i.e, Ethics Committee of Kayseri City Hospital (decision number: 520) was approved the study and conducted according to the Helsinki Declaration.

Data Statement

The data used to support the findings of this study are available on request from the corresponding author.

References

1. Cnattingius S, Villamor E, Johansson S, et al. Maternal obesity and risk of pretermdelivery. Jama. 2013 Jun 12;309(22):2362-70.

2. Sahin E, Madendag Y, Sahin ME, et al. New ultrasonographic midtrimester scoringmethod for predicting spontaneous preterm birth in uncomplicated asymptomatic twinpregnancies. Journal of Perinatal Medicine. 2022.

3. Roberts D, Brown J, Medley N, et al. Antenatal corticosteroids for accelerating fetallung maturation for women at risk of preterm birth. The Cochrane database ofsystematic reviews. 2017 Mar 21;3(3):Cd004454.

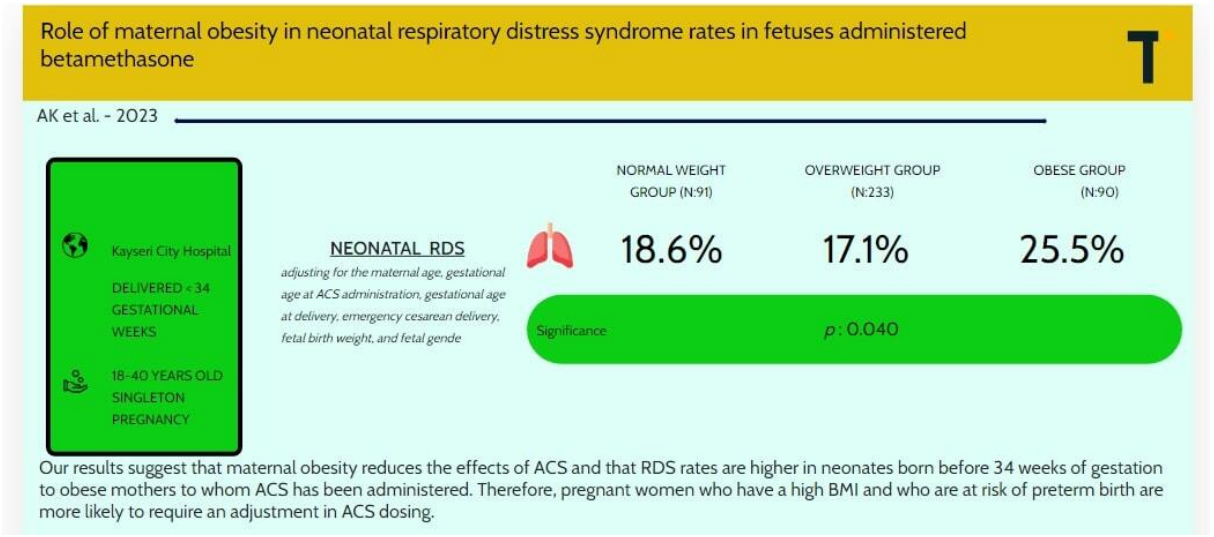
4. Committee Opinion No. 713: Antenatal Corticosteroid Therapy for Fetal Maturation.Obstet Gynecol. 2017 Aug;130(2):e102-e109. 5. Hanley MJ, Abernethy DR, Greenblatt DJ. Effect of obesity on the pharmacokinetics

of drugs in humans. Clinical pharmacokinetics. 2010;49(2):71-87.

6. Skoll A, Boutin A, Bujold E, et al. No. 364-Antenatal Corticosteroid Therapy forImproving Neonatal Outcomes. Journal of obstetrics and gynaecology Canada : JOGC= Journal d'obstetrique et gynecologie du Canada : JOGC. 2018 Sep;40(9):1219-1239.

7. Hofer OJ, McKinlay CJD, Tran T, et al. Antenatal corticosteroids, maternal body massindex and infant morbidity within the ASTEROID trial. The Australian & NewZealand journal of obstetrics & gynaecology. 2021 Jun;61(3):380-385.
8. Bonanno C, Wapner RJ. Antenatal corticosteroids in the management of preterm birth:are we back where we started? Obstetrics and gynecology clinics of North America.2012 Mar;39(1):47-63.
9. Della Torre M, Hibbard JU, Jeong H, et al. Betamethasone in pregnancy: influence ofmaternal body weight and multiple gestation on pharmacokinetics. Am J Obstet Gynecol. 2010 Sep;203(3):254.e1-12.
10. Faden M, McDonald SD, Shah PS, et al. Impact of antenatal corticosteroids in preterm neonates based on maternal body mass index. Journal of perinatology : official journal of the California Perinatal Association. 2018 Jul;38(7):813-819.
11. Hashima JN, Lai Y, Wapner RJ, et al. The effect of maternal body mass index onneonatal outcome in women receiving a single course of antenatal corticosteroids. AmJ Obstet Gynecol. 2010 Mar;202(3):263.e1-5.
12. Gordijn S, Beune I, Thilaganathan B, et al. Consensus definition of fetal growthrestriction: a Delphi procedure. Ultrasound in Obstetrics & Gynecology.2016;48(3):333-339.
13. Eraslan Sahin M, Sahin E, Col Madendag I, et al. Evaluation of midtrimester ductusvenosus diameter and peak systolic velocity to predict late onset small for gestationalage fetuses. The Journal of Maternal-Fetal & Neonatal Medicine. 2020:1-7.
14. Büke B, Destegül E, Akkaya H, et al. Prediction of neonatal respiratory distress syndrome via pulmonary artery Doppler examination. The journal of maternal-fetal &neonatal medicine: the official journal of the European Association of PerinatalMedicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2019 May;32(10):1640-1645.
15. Claire L, Vieux R. Efficacy of antenatal corticosteroids according to maternal andperinatal factors: a retrospective cohort study. Am J Perinatol. 2015 Sep;32(11):1070-
16. Vricella LK, Louis JM, Chien E, et al. Blood volume determination in obese andnormal-weight gravidas: the hydroxyethyl starch method. Am J Obstet Gynecol. 2015Sep;213(3):408.e1-6.
17. Watterberg KL, Ballard PL. Optimizing antenatal corticosteroid therapy for improvingoutcome of premature infants. Pediatric research. 2019 Nov;86(5):556-557.

18. Schmidt AF, Jobe AH, Kannan PS, et al. Oral antenatal corticosteroids evaluated infetal sheep. Pediatric research. 2019 Nov;86(5):589-594.
19. Kuk, Jin-Yi, et al. "Optimal time interval between a single course of antenatal corticosteroids and delivery for reduction of respiratory distress syndrome in preterm twins." *American journal of obstetrics and gynecology* 209.3 (2013): 256-e1.
20. Yasuhi, Ichiro, et al. "Influence of the interval between antenatal corticosteroid therapy and delivery on respiratory distress syndrome." *Journal of Obstetrics and Gynaecology Research* 43.3 (2017): 486-491


Role of maternal obesity in neonatal respiratory distress syndrome rates in fetuses administered betamethasone
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Kayseri City Hospital
DELIVERED < 34 GESTATIONAL WEEKS
18-40 YEARS OLD SINGLETON PREGNANCY
NEONATAL RDS
adjusting for the maternal age, gestational age at ACS administration, gestational age at delivery, emergency cesarean delivery, fetal birth weight, and fetal gende
NORMAL WEIGHT GROUP (N:91)
OVERWEIGHT GROUP (N:233)
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18.6%
17.1%
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Significance
p: 0.040
Our results suggest that maternal obesity reduces the effects of ACS and that RDS rates are higher in neonates born before 34 weeks of gestation to obese mothers to whom ACS has been administered. Therefore, pregnant women who have a high BMI and who are at risk of preterm birth are more likely to require an adjustment in ACS dosing.

Table1. Maternal demographic characteristics of the study groups.

Characteristic	**Normal Weight Group(n:91)**	**Overweight Group(n:233)**	**Obese Group (n:90)**	**PValue**
Maternal age(year)	23.4 ± 2.6	27.4 ± 3.4	30.4 ± 3.1	<0.001
BMI at ACS administration(kg/m^2)	24.2 ± 0.7	27.3 ± 2.1	32.9 ± 2.1	<0.001
Parity	1(1–2)	2(2–3)	2(2–3)	<0.001
Ethnicity(Caucasian)	83(91.2)	209(89.6)	82(91.1)	0.820
Previous caesarean Delivery	22(24.1)	60(25.7)	19(21.1)	0.640

Notes: BMI, body mass index; ACS, antenatal corticosteroid. The data are presented as the mean ± standard deviation, median(25^{th}–75^{th} percentile), or n(%).

Table2. Perinatal outcomes and neonatal respiratory distress syndrome (RDS) rates of the study groups.

Characteristic	**Normal Weight Group(n:91)**	**Overweight Group (n:233)**	**Obese Group (n:90)**	**PValue**	**Adjusted p-value**
Gestational age at ACS administration (week)	30(28-31)	30(29-31)	31(30-31)	0.494	
Gestational age at Delivery (week)	32(31-32)	32(31-33)	32(32-33)	0.642	
Interval between administration of ACS and delivery -48-72 hour - 72 hour- 7 day - More than 7 days	 19 (20.8) 54 (59.3) 18 (19.9)	 41 (17.6) 141 (60.6) 51 (21.8)	 21 (23.3) 58 (64.4) 11 (12.2)	0. 820	
Emergency Caesarean delivery rate - Fetal distress - Obstructed labor - Umbilical cord prolapses - Unexplained vaginal hemorrhage	7 (7.6) 6 (6.5) 1 (1.0) 0 (0) 0 (0)	16 (6.9) 12 (5.1) 2 (0.8) 1 (0.4) 1 (0.4)	6(6.6) 5 (5.5) 1 (1.1) 0 (0) 0 (0)	0.560	
Fetal birth weight (g)	1880 ± 560	1900 ± 550	1980 ± 510	0.150	

Birth weight percentile	58(52–68)	64(60–69)	68(62–74)	0.820	
Malesex	51(56.1)	135(57.9)	48(53.3)	0.612	
5-min Apgar score	8(8–9)	9(9–10)	9(9–10)	0.960	
Presence of neonatal RDS	17(18.6)	40(17.1)	23(25.5)	0.040	0.032
Mean length of stay in the NICU(d)	10.2 ± 10.0	8.1 ± 17.5	8.6 ± 15.4	0.790	

Notes: ACS, antenatalcorticosteroid; RDS, respiratory distress syndrome; NICU, neonatal intensive care unit; NA, not available. The data are presented as the mean±standard deviation, median (25^{th}–75^{th}percentile), orn(%).

Neonatal RDS rates were adjusted for the Maternal age, gestational age at ACS administration, gestational age at delivery, emergency caesarean delivery, fetal weight and male fetal gender.

Figure 1. Flow chart of study population.