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Factors influencing neonatal outcomes in twin pregnancies undergoing cesarean section: a cross-sectional study

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SUMMARY

OBJECTIVE: This study aimed to evaluate maternal and fetal characteristics and factors affecting fetal outcomes in twin pregnancies delivered by cesarean section.

METHODS: This was a cross-sectional study in a tertiary care referral hospital. The primary outcome was to ascertain the effects of independent factors on the 1st and 5th minute APGAR scores, neonatal intensive care unit admissions, the need for mechanical ventilation, and neonatal mortality.

RESULTS: A total of 453 pregnant women and 906 newborns were included in the analysis. The final logistic regression model revealed that early gestational weeks and neonates <3rd weight percentile at the time of delivery were the most significant predictors of all poor outcome parameters in at least one of the twins ($p<0.05$). General anesthesia for cesarean section was associated with 1st minute APGAR<7 and the need for mechanical ventilation, and emergency surgery was correlated with the need for mechanical ventilation ($p<0.05$) in at least one of the twins.

CONCLUSION: General anesthesia, emergency surgery, early gestational weeks, and birth weight <3rd weight percentile were strongly associated with poor neonatal outcomes in at least one of the twins delivered by cesarean section.

KEYWORDS: Anesthesia, obstetrical. Pregnancy twin.

INTRODUCTION

While the rate of multiple pregnancies varies significantly among societies and individuals, it has shown a significant rise worldwide, especially in middle- and high-income countries. The growing use of assisted reproductive procedures due to increased maternal age and decreased fertility is another factor contributing to multiple pregnancies[1]. As a result, multiple pregnancies constitute approximately 2–4% of all births[2].

Multiple pregnancies are associated with greater maternal and fetal risks compared to singleton pregnancies[3]. The maternal mortality associated with a twin pregnancy is 2.5 times higher than that for a singleton pregnancy[4], and adverse neonatal outcomes such as perinatal mortality, fetal growth restriction, and low birth weight are two to three times higher among twins[5]. Moreover, neonatal near-miss, which refers to cases that almost resulted in death, has been found to be associated with multiple pregnancies[6,7].

However, cesarean delivery is associated with a higher risk of maternal morbidity and poor neonatal outcomes[8,9]. From this perspective, we aimed to evaluate maternal and fetal characteristics and factors affecting fetal outcomes in twin pregnancies delivered by cesarean section.

METHODS

After the approval of the local Ethics Committee (2011-KAEK-25 2019/05-26), our study was conducted following the principles of the Declaration of Helsinki. The study was registered at www.clinicaltrials.gov under the number NCT05104255. This single-center, cross-sectional chart review comprised twin pregnancies and newborns delivered by cesarean section. The main a priori objective was to evaluate four outcome parameters among neonates: APGAR scores, neonatal intensive care unit (NICU) admissions, the need for non-invasive or invasive mechanical ventilation (MV), and neonatal death. We then analyzed mothers' and newborns' demographic data and characteristics from the electronic medical records. Multiple pregnancies involving triplets or more and twins delivered through the vaginal route were excluded. All neonates were examined by a neonatologist in the operating room after delivery.

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General anesthesia was applied to patients with emergency Category 1 (which means "immediate threat to the life of the mother or baby")[10], when there was not enough time for regional anesthesia. Spinal anesthesia was administered through the L3-4 or L4-5 interspinous space with a 25G Quincke spinal needle by injecting 10–12 mg of hyperbaric bupivacaine, following the free flow of the cerebrospinal fluid. Ephedrine (5–10 mg) was administered intravenously if the blood pressure fell 20% or more below the baseline. Propofol (2–2.5 mg/kg) and rocuronium (0.6–1 mg/kg) were used for induction. Fentanyl (1 μg/kg) was administered immediately after clamping the cord, and then the anesthesia was continued with sevoflurane (1–2%) in an oxygen and air mixture.

Maternal age, predelivery body mass index (BMI), parity, gestational age at delivery, emergency of the cesarean section, anesthesia method, use of intraoperative antihypotensive agents (ephedrine), preoperative and intraoperative use of blood products, and neonatal weight percentile distribution for a given gestational age at delivery were considered as independent variables affecting neonatal outcomes. The primary outcome of the study was to ascertain the effects of independent factors on poor outcomes in newborns. A newborn was considered to have a poor outcome if any of the following variables were present: 1st and 5th minute APGAR scores<7, NICU admission, need for non-invasive or invasive MV, or neonatal mortality within the first 28 days after birth.

The data of the neonates included in the correlation analysis and multivariate logistic regression models were dichotomized as 0 (none of the twins) or 1 (at least one of the twins). The neonatal weight percentile distribution for a given gestational age at delivery was categorized as <3rd weight percentile or ≥3rd weight percentile. The APGAR scores at the 1st and 5th minutes were dichotomized as APGAR scores <7 or ≥7.

The statistical data were analyzed using the SPSS Statistics for Windows, version 19.0, 2010 (IBM Corp., Armonk, NY). The normality of the distribution was analyzed with the Shapiro-Wilk test. The patients' demographic and clinical characteristics are presented as median (min–max) and frequency (proportion). Pearson's chi-squared test was used to compare the categorical variables, and the Mann-Whitney U test was performed to compare the continuous variables. A nonparametric Spearman test was conducted to determine the associations between maternal and neonatal factors. Accordingly, a logistic regression model was built, and a multivariate analysis was performed for each significant factor influencing neonatal outcomes as determined by the correlation analysis. After the multicollinearity analysis (tolerance>0.4), the Hosmer-Lemeshow test was run to check the model's fitness. The effect sizes are presented as odds ratios (OR) and 95% confidence intervals (CIs). All tests were performed with two-tailed, and $p<0.05$ was considered significant.

RESULTS

Between January 2017 and January 2020, 478 (86.7%) of 551 multiple pregnancies were delivered by cesarean section. Triplets and more (4 patients), and patients with a congenital anomaly in at least one of the twins (21 patients) that were delivered by cesarean section were excluded from the study. Accordingly, a total of 453 pregnant women and 906 newborns were included in the further analysis.

The general characteristics of the patients are presented in Table 1. The median gestational week at the time of delivery was 35 (min. 24 to max. 39) weeks.

Table 1 shows the intraoperative care characteristics and complications during pregnancy and delivery. Of 453 (68.9%), 312 patients underwent emergency cesarean section, and of 453 (81.5%), 369 women received spinal anesthesia. Six patients who received combined spinal and epidural anesthesia were included in the spinal anesthesia group because no additional drugs were administered through epidural catheters during the surgery. No maternal mortality was observed in the following postoperative 1-month period.

Table 2 shows the comparison of physical characteristics, APGAR scores at delivery, and data regarding poor outcomes for the first- and second-born twins. The second-born twins had a significantly lower birth weight than the first-born twins ($p=0.008$). Also, the number of neonates with <3rd weight percentile was significantly higher among the second-born twins than the first-born twins ($p=0.001$). However, we found no difference between the first- and second-born neonates in terms of poor outcomes. According to the correlation analysis, which was performed for fetal and maternal parameters that were considered to affect neonatal outcomes, early gestational weeks, emergency surgery, general anesthesia administration for cesarean section, and neonates <3rd weight percentile were correlated with the predetermined poor neonatal outcomes ($p<0.01$). Among these parameters, the early gestational weeks strongly correlated with NICU admissions ($r=0.566$) and the need for MV ($r=0.534$). Besides, early gestational weeks had a moderate correlation with the 1st and 5th minute APGAR scores ($r=0.430$ and 0.322, respectively) and neonatal mortality ($r=0.365$).

The significant parameters from the correlation test were included in the final regression model (Table 3). The logistic regression was repeated to ascertain the effects of spinal anesthesia, gestational weeks, emergency surgery, and neonates <3rd

Table 1. Patient characteristics and perioperative care characteristics.

Age, years; median (min–max)	28 (15–48)
Weight, kg; median (min–max)/ Height, cm; median (min–max)	80 (56–121)/160 (150–175)
BMI, kg m^{-2}; median (min–max)	31.2 (21.9–50.4)
Gravidity, n; median (min–max)/ Parity, n; median (min–max)	2 (1–10)/1 (0–9)
Gestational weeks, weeks; median (min–max)	35 (24–39)
Extreme preterm; 24 (+0) –27 (+7); n (%)	18 (4.0)
Very early preterm; 28 (+0)–31 (+7); n (%)	52 (11.5)
Early preterm; 32 (+0) –33 (+7); n (%)	51 (11.3)
Late preterm; 34 (+0)–36 (+7); n (%)	233 (51.4)
Early term and term; >37 (+0); n (%)	99 (21.9)
Platelet count, mcl; median (min–max)	202 (37–539)
Hemoglobin, g dL^{-1}; median (min–max)	11 (6.3–15)
Anemia; <11 g dL^{-1}; n (%)	197 (43.5)
Comorbidities; n (%); Thyroid disease	12 (2.7)
Hypertension	9 (2.0)
Diabetes mellitus	6 (1.3)
Other*	9 (1.9)
Perioperative care characteristics and complications during pregnancy and delivery.	
Surgical admission; n (%); Emergent/ Elective	312 (68.9)/141 (31.1)
Anesthesia method; n (%); Spinal/ General	369 (81.5)/84 (18.5)
Intraoperative ephedrine use; n (%)	147 (32.5)
Postoperative follow-up; n (%); Ward/ ICU	430 (94.9)/23 (5.1)
Complications during pregnancy and delivery; n (%)	
Preeclampsia	22 (4.9)
Gestational diabetes mellitus	18 (4.0)
Premature rupture of membranes	7 (1.6)
Other**	22 (4.9)
Duration of surgery, min; median (min–max)	50 (30–90)
Intraoperative bleeding, mL; median (min–max)	300 (100–1200)
Blood products; n (%)	53 (11.7)
Hospital stay time, days; median (min–max)	3 (1–13)

BMI: body mass index. Other*: Familial Mediterranean fever, facial paralysis, epilepsy, chronic respiratory disease. ICU: intensive care unit. Other**: uterine atony, uterine rupture, rectus sheath hematoma, placental abruption, vaginal bleeding, cholestasi.

weight percentile on each individual dependent factor: APGAR 1st minute <7, APGAR 5th minute <7, NICU admission, the need for MV, and neonatal death. The model for APGAR 1st minute <7 correctly classified 90.7% of the cases with a specificity of 97.7% (R^2=0.470); the model for APGAR 5th minute <7 correctly classified 95.1% of the cases with a specificity of 98.4% (R^2=0.452); the model for NICU admission correctly classified 81.7% of the cases with a specificity of 89.8% (R^2=0.542); the model for the need for MV correctly classified 87.6% of the cases with a specificity of 95.6% (R^2=0.558); and the model for neonatal death correctly classified 94.7% of the cases with a specificity of 98.1% (R^2=0.499). Early gestational weeks and neonates <3rd weight percentile at the time of delivery were found to be the most significant predictors of all poor outcome parameters in at least one of the twins ($p<0.05$). General anesthesia was associated with APGAR 1st minute <7 and the need for MV ($p<0.05$), and emergency surgery showed an association with the need for MV ($p<0.05$).

Table 2. Characteristics of the twins.

	1st twin	2nd twin	p
Weight; median (min–max)	2320 (450–3680)	2200 (470–3650)	0.008*
Height; median (min–max)	46 (24–52)	46 (24–54)	0.057
Gender; n (%)			
Women/man	230 (50.8)/223 (49.2)	233 (51.4)/220 (48.6)	0.894
Weight percentiles; n (%)			
<3rd	45 (9.9)	85 (18.8)	0.001*
3rd–10th	64 (14.1)	56 (12.4)	
>10th	344 (75.9)	312 (68.9)	
APGAR scores <7; n (%)			
1st minute	36 (7.9)	43 (9.5)	0.480
5th minute	15 (3.3)	15 (3.3)	1
APGAR scores <7 in general anesthesia (n=84); n (%)			
1st minute	15 (17.9)	17 (20.2)	0.694
5th minute	8 (9.5)	7 (8.5)	0.073
NICU admission; n (%)	176 (38.9)	193 (42.6)	0.279
Non-invasive and invasive MV; n (%)	74 (16.3)	79 (17.4)	0.723
Intubated in the operating room; n (%)	50 (8.8)	48 (10.6)	0.432
Died within the first 28 days; n (%)	20 (4.4)	24 (5.3)	0.536

*p<0.05; MV: mechanical ventilation; NICU: neonatal intensive care unit.

Table 3. Logistic regression analysis of the significant independent factors.

	Spinal anesthesia	Gestational weeks	Emergent surgery	<3rd percentile
APGAR 1st min <7				
OR, [95%CI]	0.356, [0.163, 0.776]	0.622, [0.553, 0.699]	1.621, [0.554, 4.739]	3.778, [1.744, 8.185]
Wald	6.744	62.952	0.779	11.355
p	0.009*	0.000*	0.378	0.001*
APGAR 5th min <7				
OR, [95%CI]	0.530, [0.183, 1.537]	0.636, [0.551, 0.734]	2.647, [0.315, 22.257]	5.678, [1.957, 16.473]
Wald	1.365	38.268	0.803	10.212
p	0.243	0.000*	0.370	0.001*
NICU				
OR, [95%CI]	0.925 [0.488, 1.754]	0.455, [0.384, 0.539]	1.456, [0.837, 2.533]	7.144, [3.898, 13.093]
Wald	0.057	82.913	1.769	40.461
p	0.811	0.000*	0.184	0.000*
MV				
OR, [95%CI]	0.420, [0.202, 0.875]	0.563, [0.493, 0.642]	4.178, [1.446, 12.075]	5.699, [2.785, 11.661]
Wald	5.364	73.524	6.975	22.691
p	0.021*	0.000*	0.008*	0.000*
Death				
OR, [95%CI]	0.772, [0.271, 2.196]	0.591, [0.510, 0.684]	1.391, [0.281, 6.896]	5.263 [1.934, 14.321]
Wald	0.236	49.641	0.163	10.573
p	0.627	0.000*	0.686	0.001*

*p<0.05. CI: confidence interval; min: minute; MV: mechanical ventilation; NICU: neonatal intensive care unit; OR: odds ratio.

DISCUSSION

The main finding of this study was that general anesthesia administration for cesarean section, early gestational weeks, emergency surgery, and neonates <3rd weight percentile were the strongest predictors for any of the poor neonatal outcomes in at least one of the twins delivered by cesarean section.

Planned cesarean section was found to be associated with increased poor neonatal outcomes between the 32nd and 37th gestational weeks[8,11-13]; on the contrary, cesarean section was suggested to be safer after 37 weeks of gestation[14]. Despite this evidence, the cesarean section rate for twin pregnancies is still very high, which may be due to preconceptions that a cesarean section may prevent inevitable complications and medico-legal issues[12].

Yielding data suggests using regional anesthesia for cesarean sections for better neonatal outcomes[15,16]. Theoretically, prolonging the inter-delivery interval during general anesthesia could have worsened the APGAR scores of second-born twins; however, in contrast to our expectations, no significant difference was found between the first and second-born twins in terms of APGAR scores. On the contrary, when all twins were taken into account, general anesthesia was positively correlated with low 1st and 5th minute APGAR scores, a higher need for MV and NICU admissions, and a higher neonatal mortality rate. Regional anesthesia was the first choice for obstetrical anesthesia. However, general anesthesia was mainly applied to patients with emergency Category 1. Thus, the reason for poor outcomes related to general anesthesia is more likely associative than causative.

Neonatal near-misses enable identifying the group of newborns who have a high risk of death due to morbidity but who survive the first 27 days of life under these conditions. Generally, the criteria of birth weight <1,750 g, 5th minute APGAR score <7, and gestational age <33 (+7) weeks were recommended for defining neonatal near-miss[17]. Previous studies found a relationship between advanced maternal age and neonatal near-miss in nulliparous and multiparous women[6]. In addition, it was stated that neonatal near-miss risk in twins was associated with parity, an early gestational week, and intrauterine growth restriction[18]. Although maternal age affects the prevalence of twins, it does not appear to affect twin pregnancy outcomes; furthermore, the preterm birth risk was higher among younger mothers[19]. In the present study, we observed that maternal age, parity, and predelivery BMI did not affect neonatal outcomes. Also, general anesthesia administration, early gestational weeks, emergency surgery, and neonates <3rd weight percentile at the time of delivery were the strongest predictors of any of the poor neonatal outcomes.

Spontaneous or medically indicated preterm birth complicates twin pregnancies[1]. Fetal lung maturation is mostly completed in the 32 weeks of gestation; births before 32 weeks have high rates of perinatal morbidity and mortality; and preterm infants from multiple births are at increased risk compared with singletons born at the same gestational age[4,5,17]. In the present study, early gestational weeks were strongly correlated with the need for MV and NICU admissions. Early gestational weeks also showed a moderate correlation between 1st and 5th minute APGAR scores and neonatal death. Therefore, efforts should be intensified to prevent avoidable twin pregnancy complications like preterm labor to achieve better neonatal outcomes.

Previous studies suggested that second-born twins had worse outcomes than first-born twins regardless of the route of delivery[2]. Besides, Luo et al. attributed the increased mortality risk of the second-born twin to their relatively smaller birth weight than the first-born twin[20]. We also found that the second-born twins had significantly lower weight percentiles and median birth weights compared to the first-born twins. While neonates <3rd weight percentile was one of the strongest factors influencing poor neonatal outcomes, we could not find a significant difference in poor outcomes between first- and second-born twins in terms, contrary to a previous study.

The main limitations of this study were the lack of data regarding assisted reproductive techniques and chorionicity. Therefore, neonates were evaluated according to their birth weight and neonatal weight percentile distribution for a given gestational age at delivery.

One strength of our research is that the number of patients included in the analysis is sufficient to show the correlation between the predetermined factors.

CONCLUSION

This study evaluated the factors associated with poor neonatal outcomes (such as low APGAR scores, NICU admissions, the need for MV, and neonatal death) among twins delivered by cesarean section. Our findings revealed that general anesthesia administration for cesarean sections, emergency surgeries, low weight percentiles, and early gestational weeks was correlated with the aforementioned variables of poor neonatal outcomes in at least one of the twins. Still, the order of birth did not affect neonatal outcomes.

AVAILABILITY OF DATA AND MATERIAL

All the data generated or analyzed during this study are included in this article.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was performed in line with the principles of the Declaration of Helsinki. Ethical approval for this study (Ethical Committee protocol No. 2011-KAEK-25) was provided by the Ethical Committee of Bursa Yuksek Ihtisas Training and Research Hospital in Bursa, Turkey. The study was registered at www.clinicaltrials.gov under the number NCT05104255.

AUTHORS' CONTRIBUTIONS

NK: Conceptualization, Data curation, Investigation, Methodology, Writing – original draft. **HG:** Conceptualization, Writing – original draft, Formal Analysis, Methodology. **UK:** Conceptualization, Data curation, Investigation, Methodology. **DK:** Conceptualization, Methodology, Writing – review & editing. **FNT:** Data curation, Formal Analysis, Investigation. **MG:** Writing – review & editing.

REFERENCES

1. Young BC, Wylie BJ. Effects of twin gestation on maternal morbidity. Semin Perinatol. 2012;36(3):162-8. https://doi.org/10.1053/j.semperi.2012.02.007
2. Santana DS, Surita FG, Cecatti JG. Multiple pregnancy: epidemiology and association with maternal and perinatal morbidity. Rev Bras Ginecol Obstet. 2018;40(9):554-62. https://doi.org/10.1055/s-0038-1668117
3. Cheong-See F, Schuit E, Arroyo-Manzano D, Khalil A, Barrett J, Joseph KS, et al. Prospective risk of stillbirth and neonatal complications in twin pregnancies: systematic review and meta-analysis. BMJ. 2016;354:i4353. https://doi.org/10.1136/bmj.i4353
4. National Collaborating Centre for Women's and Children's Health (UK). Multiple pregnancy: the management of twin and triplet pregnancies in the Antenatal Period. London: RCOG Press; 2011. PMID: 22855972
5. Obiechina Nj, Okolie V, Eleje G, Okechukwu Z, Anemeje O. Twin versus singleton pregnancies: the incidence, pregnancy complications, and obstetric outcomes in a Nigerian tertiary hospital. Int J Womens Health. 2011;3:227-30. https://doi.org/10.2147/IJWH.S22059
6. Martinelli KG, Gama SGND, Almeida AHDV, Pacheco VE, Santos Neto ETD. Advanced maternal age and factors associated with neonatal near miss in nulliparous and multiparous women. Cad Saude Publica. 2019;35(12):e00222218. https://doi.org/10.1590/0102-311X00222218
7. Silva GA, Rosa KA, Saguier ESF, Henning E, Mucha F, Franco SC. A populational based study on the prevalence of neonatal near miss in city located in the South of Brazil: prevalence and associated factors. Rev Bras Saúde Matern Infant.2017;17:159-67. https://doi.org/10.1590/1806-9304201700010000.
8. Schmitz T, Prunet C, Azria E, Bohec C, Bongain A, Chabanier P, et al. Association between planned cesarean delivery and neonatal mortality and morbidity in twin pregnancies. Obstet Gynecol. 2017;129(6):986-95. https://doi.org/10.1097/AOG.0000000000002048
9. Roberts CL, Algert CS, Nippita TA, Bowen JR, Shand AW. Association of prelabor cesarean delivery with reduced mortality in twins born near term. Obstet Gynecol. 2015;125(1):103-10. https://doi.org/10.1097/AOG.0000000000000578
10. National Collaborating Centre for Women's and Children's Health (UK). Caesarean section. London: RCOG. Press; 2011. PMID: 23285498
11. Barrett JF, Hannah ME, Hutton EK, Willan AR, Allen AC, Armson BA, et al. A randomized trial of planned cesarean or vaginal delivery for twin pregnancy. N Engl J Med. 2013;369(14):1295-305. https://doi.org/10.1056/NEJMoa1214939
12. Dathan-Stumpf A, Winkel K, Stepan H. Delivery of twin gestation (≥ 32.0 weeks): the vaginal route as a practicable and safe alternative to cesarean section. Geburtshilfe Frauenheilkd. 2020;80(10):1033-40. https://doi.org/10.1055/a-1181-8737
13. Aviram A, Lipworth H, Asztalos EV, Mei-Dan E, Melamed N, Cao X, et al. Delivery of monochorionic twins: lessons learned from the Twin Birth Study. Am J Obstet Gynecol. 2020;223(6):916.e1-e9. https://doi.org/10.1016/j.ajog.2020.06.048
14. Zafarmand MH, Goossens SMTA, Tajik P, Bossuyt PMM, Asztalos EV, Gardener GJ, et al. Planned cesarean or planned vaginal delivery for twins: secondary analysis of randomized controlled trial. Ultrasound Obstet Gynecol. 2021;57(4):582-91. https://doi.org/10.1002/uog.21907
15. Mancuso A, Vivo A, Giacobbe A, Priola V, Maggio Savasta L, Guzzo M, et al. General versus spinal anaesthesia for elective caesarean sections: effects on neonatal short-term outcome. A prospective randomised study. J Matern Fetal Neonatal Med. 2010;23(10):1114-8. https://doi.org/10.3109/14767050903572158
16. Karaca Ü, Özgünay ŞE, Ata F, Kılıçarslan N, Yılmaz C, Karasu D. Our experiences of anesthesia in emergency cesarean sections. JARSS. 2020;28(4):275-80. https://doi.org/10.5222/jarss.2020.9230028:275-280
17. Santos JP, Cecatti JG, Serruya SJ, Almeida PV, Duran P, Mucio Bd, et al. Neonatal near miss: the need for a standard definition and appropriate criteria and the rationale for a prospective surveillance system. Clinics (Sao Paulo). 2015;70(12):820-6. https://doi.org/10.6061/clinics/2015(12)10
18. Lopes FNB, Gouveia APM, Carvalho OMC, Júnior ABV, Leite ÁJM, Araujo Júnior E, et al. Associated factors with neonatal near miss in twin pregnancies in a public referral maternity unit in Brazil. J Turk Ger Gynecol Assoc. 2021;22(1):12-21. https://doi.org/10.4274/jtgga.galenos.2021.2020.0176
19. McLennan AS, Gyamfi-Bannerman C, Ananth CV, Wright JD, Siddiq Z, D'Alton ME, et al. The role of maternal age in twin pregnancy outcomes. Am J Obstet Gynecol. 2017;217(1):80.e1-e8. https://doi.org/10.1016/j.ajog.2017.03.002
20. Luo ZC, Ouyang F, Zhang J, Klebanoff M. Perinatal mortality in second-vs first-born twins: a matter of birth size or birth order? Am J Obstet Gynecol. 2014;211(2):153.e1-8. https://doi.org/10.1016/j.ajog.2014.02.024