Prenatal Prediction of Difficult Intubation in Periviable Neonates Using Standard Fetal Biometric Parameters

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Abstract

Objective To assess whether standard fetal biometric parameters can be used to predict difficult intubations in periviable neonates undergoing resuscitation.

Study Design This is a retrospective case–control study of periviable neonates delivered at 23 to $25^{6/7}$ weeks at an academic hospital during a 5-year period in whom intubation was attempted. Standard fetal biometric measurements were included if they were taken within 7 days of delivery. Primary outcome was intubation in one attempt and was compared with more than one attempt. Data were also collected for fetal gestational age at delivery, neonatal birth weight, estimated fetal weight, head circumference, biparietal diameter, and abdominal circumference. Parametric and nonparametric statistical tests used $p < 0.05$ as significant.

Results In total, 93 neonates met the inclusion criteria. The mean estimated fetal weight was 675 g (standard deviation [SD] ± 140), and the mean neonatal birth weight was 706 g (SD ± 151). The median interval between fetal ultrasound and delivery was 3 days (range: 0–7 days). A total of 45 neonates (48.3%) required more than one intubation attempt. The median number of intubation attempts was 1 (range: 1–10). There was no association between intubation difficulty and fetal abdominal circumference, biparietal diameter, head circumference, gestational age, estimated fetal weight, and neonatal birth weight (all $p > 0.05$).

Conclusion Standard biometry in periviable neonates does not predict intubation difficulty.

Keywords
- periviable
- intubation
- preterm birth
- biometry

In 2015, the rate of preterm birth in the United States was 9.6%.[1] Although periviable birth from $20^{0/7}$ to $25^{6/7}$ weeks[2] represents the minority of preterm deliveries, the survival rate of these neonates continues to increase. A 2017 National Institute of Child Health and Human Development Neonatal Research Network study of 11 centers across the United States reported a survival rate of 24% at 23 weeks and 55% at 24 weeks.[3] These severely preterm neonates have a wide range of morbidity and mortality, and most neonates will require intubation for adequate respiration.[4] Regardless of gestational age, neonatal intubation is associated with a high rate of complications such as esophageal intubation, hypotension, airway trauma, aspiration, laryngospasm, and cardiac arrest.[5] Severe complications occur in 22 to 39% of neonatal intubation attempts, and the number of attempts is associated with a higher rate of adverse events.[6,7] Intubation can be even more technically challenging in periviable or extremely low birth weight infants. One study in extremely low birth weight infants ≤ 1,000 g, which included periviable deliveries, demonstrated that multiple intubation attempts were associated with a 53% rate of death or neurodevelopmental impairment versus 29% in neonates intubated with the first attempt.[8]

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Because survival may depend on successful intubation, a means of predicting intubation difficulty prior to delivery may aid in decisions regarding how aggressive to be obstetrically and with resuscitation. This is especially important because there is mounting evidence that certain interventions are associated with an increased risk of adverse outcome in future pregnancies. For example, periviable cesarean sections are associated with a greater risk of uterine rupture, regardless of the type of uterine incision.[9] As such, prenatal factors that predict neonatal outcome could potentially play a large role in providing comprehensive and appropriate care to these women and their infants, especially in instances where families may choose comfort care. We hypothesize that standard fetal biometric measurements, particularly head circumference (HC), are proportional to the fetal trachea size and thereby facilitate prediction of difficult delivery room intubations in extremely preterm neonates.

Materials and Methods

We performed a retrospective case–control study of neonates delivered from January 1, 2011 to December 31, 2016, at the University of Rochester Medical Center, a referral center with a level III neonatal intensive care unit (NICU). All neonates delivered at $23^{0/7}$ to $25^{6/7}$ weeks' gestation were identified through the birth certificate and NICU databases. As an institutional policy, only pregnancies $\geq 23^{0/7}$ weeks' gestation were offered neonatal resuscitation. All infants without known fetal anomalies, in whom resuscitation and intubation were attempted, and for whom sonographic biometry had been performed by certified ultrasonographers within 7 days were included. The primary outcome was the number of intubation attempts in the delivery room prior to transfer to the NICU. Intubation in one attempt was compared with cases requiring more than one intubation attempt.

Each neonatal outcome was individually counted, although in multiple gestations, maternal data (age, ethnicity, body mass index, infertility treatments, antenatal corticosteroids, diabetes, hypertension, renal disease, mode of delivery, and tobacco use) were included only once. Data were also collected for fetal gestational age at delivery, neonatal birth weight, estimated fetal weight (EFW), HC, biparietal diameter (BPD), and abdominal circumference (AC). HC and BPD were measured on a transverse view of the fetal head at the level of the thalamus, cavum septum pellucidum, and falx cerebri. AC was measured on a transverse view of the fetal abdomen at the level of the portal vein and stomach. EFW was calculated using Hadlock's formula. Secondary neonatal outcomes including neonatal death, grade 3/4 interventricular hemorrhage, necrotizing enterocolitis, periventricular leukomalacia, chest compressions, epinephrine administration, bronchopulmonary dysplasia, and length of NICU admission were also recorded. Posthoc power analysis determined that our study population had 80% power (two-tailed $\alpha = 0.05$) to detect a difference in HC between groups of 8 mm at 23 weeks and 13 mm at 24 and 25 completed weeks' gestation. This corresponds to the HC difference between the 25th and 75th percentiles at 24 and 25 weeks' gestational age. Fisher's exact test, χ^2 test, and Mann–Whitney *U*-tests were performed as appropriate, with $p < 0.05$ considered significant (IBM SPSS Statistics 24.0, IBM Corp., Armonk, NY) Institutional Review Board approval was obtained from the University of Rochester Medical Center prior to study initiation. Patient consent was not required as this was a retrospective study. The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines were referenced and closely followed.

Results

Of 186 neonates, a total of 16 (8.6%) did not undergo active resuscitation based on the physician–patient joint decision for no resuscitation; of these, 12 (75%) were born at 23 to $23^{6/7}$ weeks and 4 (25%) were born at 24 to $24^{6/7}$ weeks. Five (2.7%) of the 186 neonates did not require intubation in the delivery room. All were transferred to the NICU with continuous positive airway pressure (one required intubation upon arrival to the NICU, two on day 2 of life, one on day 6 of life, and one did not require intubation). The infant that did not require intubation was a 705-g female born at $25^{1/7}$ weeks and had received a full course of antenatal corticosteroids (►**Fig. 1**).

Of the 186 periviable deliveries, 93 neonates met the inclusion criteria: 21 (22.6%) were born at 23 to $23^{6/7}$ weeks, 27 (29%) were born at 24 to $24^{6/7}$ weeks, and 45 (48.4%) were born at 25 to $25^{6/7}$ weeks (►**Fig. 2**). A total of 69 (74.2%) were singletons and 24 (25.2%) twins. The mean EFW was 675 g (standard deviation [SD] ± 140 g) and mean neonatal birth

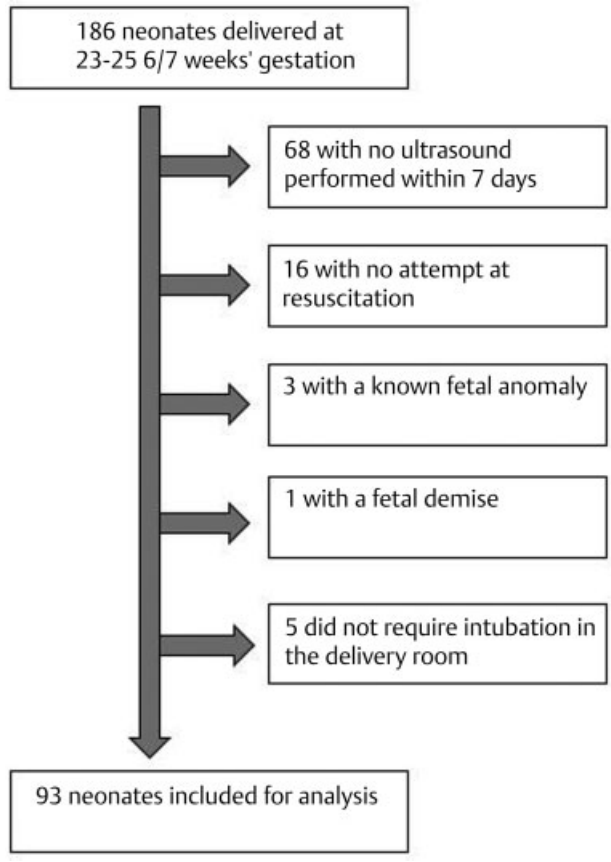

Fig. 1 Inclusion and exclusion criteria.

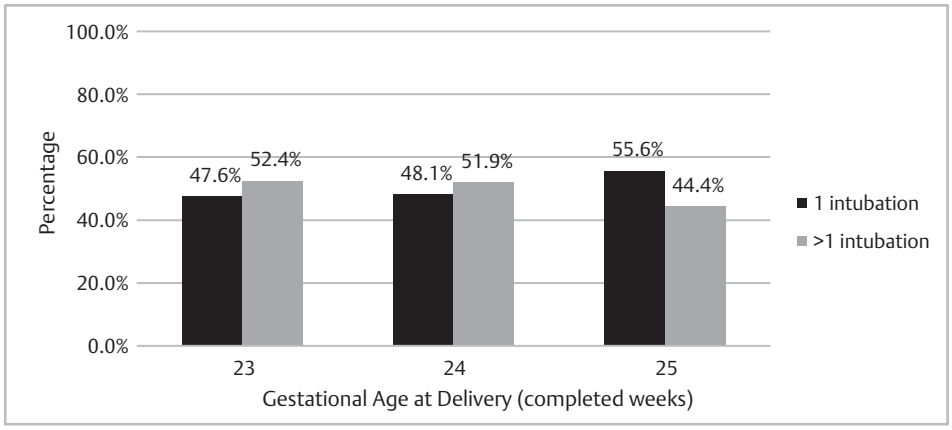

Fig. 2 Intubation attempts based on gestational age.

weight was 706 g (SD ± 151 g). There was no difference in maternal demographic or delivery characteristics between groups (►**Table 1**).

Overall, 48 (5.16%) neonates' required only one attempted intubation in the delivery room. Of those that required more than one intubation attempt, 23 (51.1%) required two, 11 (24.4%) required two, 6 (13.3%) required four, and only four (8.8%) required more than five intubation attempts. One 570-g male born at $24^{1/7}$ weeks with an HC in the 35th percentile for gestational age who had completed a course of betamethasone required a total of 10 intubation attempts. Median gestational age at delivery was $24^{6/7}$ weeks (range: $23^{0/7}$–$25^{6/7}$), and the median number of intubation attempts was 1 (range: 1–10). The median interval between the fetal ultrasound and delivery was 3 days (range: 0–7). There was no association between fetal HC and more than one intubation attempt (13.5 vs. 14%, $p = 0.99$), nor was there any association between fetal AC, BPD, EFW, or birth weight, and more than one intubation (►**Table 2**). Gestational age at delivery also had no association with more than one intubation attempt (52.4% at 23 weeks, 51.9% at 24 weeks, and 44.4% at 25 weeks; $p = 0.54$) (►**Fig. 2**). When stratified by gestational age, there was no association between HC and intubation difficulty at 23, 24, or 25 weeks' gestation (►**Table 3**). There also was no association with intubation difficulty when analyzing each gestational age strata according to HC percentile ≤10% or ≤25% (►**Table 3**).

In evaluating neonatal outcomes, the administration of epinephrine was associated with more than one intubation attempt (6.3 vs. 28.9%; $p = 0.004$). There were no significant differences in neonatal death, grade 3/4 interventricular hemorrhage, necrotizing enterocolitis, periventricular leukomalacia, chest compressions, and bronchopulmonary dysplasia based on intubation attempts. However, there was a trend toward a higher rate of neonatal adverse outcomes with more than one intubation attempt that did not reach statistical significance (►**Table 4**).

Discussion

Overall, there was no association between standard fetal biometric measurements (HC, BPD, AC, and EFW) and intubation difficulty during the initial resuscitation of a periviable neonate. We also did not observe an association between gestational age at delivery or birth weight and intubation difficulty. This finding may be a reflection of the inclusion criteria for the study which required that neonates have plans for active resuscitation and intubation attempted. As such, for neonates not considered candidates for active resuscitation, possibly with smaller biometry, there was no data on the difficulty of intubation because it was not attempted. In our study, neonates born at ≥ $23^{0/7}$ weeks' gestation without active resuscitation represented only 8.6% of all periviable deliveries. Therefore, although this may have had some impact, it is unlikely to have influenced the results significantly.

In this study, a total of 48.3% of neonates born at 23 to $25^{6/7}$ weeks' gestation required more than one intubation attempt. In one study, 60% of extremely low birth weight neonates (less than 1,000 g) required multiple attempts to achieve a successful intubation.[8] Although we did not observe an association of biometric parameters or gestational age with intubation difficulty, we did observe a trend that more neonates at 23 and 24 completed weeks' gestation required more than more than one intubation attempt, as compared with those at 25 completed weeks. However, the magnitude of this difference was small and clinically insignificant. Our study was powered to detect a difference in HC of 8 to 13 mm between groups and differences within the normal range of HCs at 23 to 25 weeks. However, our results may not have demonstrated an association with fetal weight or gestational age of delivery because intubation difficulty may be more evident at earlier gestational age (e.g., 22 weeks, before aggressive resuscitation is undertaken at our site) and lower birth weight than is reflected in this study. In our study, only six neonates had a birth weight less than 500 g, and there were no neonates of <23 weeks' gestational age who had active resuscitation.

We did observe that epinephrine administration was associated with more than one intubation attempt. Epinephrine use does not directly affect intubation difficulty but instead is likely a marker for a difficult neonatal resuscitation.[10] There is evidence that very low birth weight (≤1,500 g), extremely preterm infants (24–27 weeks' gestational age) who require delivery room cardiopulmonary resuscitation have a higher rate of adverse neonatal outcome, including mortality, grade 3/4 intraventricular hemorrhage, and periventricular leukomalacia.[11]

Table 1 Demographic data

	One intubation attempt ($n = 48$)	More than one intubation attempt ($n = 45$)	*p*-Value
Median maternal age	27.5 (23.2–32)	27.5 (22.7–33)	0.77[a]
Twin gestation	15 (31.3)	9 (20)	0.22
Infertility treatments	4 (10)	3 (7.7)	0.72
Ethnicity			0.42
Caucasian	23 (56.1)	28 (70)	
African-American	13 (31.7)	10 (25)	
Hispanic	3 (7.3)	0 (0)	
Asian	1 (2.4)	1 (2.5)	
Other	1 (2.4)	1 (2.5)	
Median body mass index (kg/m^2)	31.3 (21–63.7)	32.5 (21.3–53)	0.84[a]
Antenatal corticosteroids			0.74[b]
None	0 (0)	0 (0)	
One dose	4 (8.3)	5 (11.1)	
Two doses	44 (91.7)	40 (88.9)	
Maternal diabetes	4 (10)	4 (10)	1[b]
Maternal hypertension	7 (17.5)	13 (32.5)	0.12
Maternal renal disease	2 (5)	2 (5)	1[b]
Neonatal sex			0.59
Male	24 (50)	25 (55.6)	
Female	24 (50)	20 (44.4)	
Mode of delivery			0.93
Vaginal delivery	18 (37.5)	18 (40)	
Low transverse cesarean	10 (20.8)	11 (24.4)	
Classical	18 (37.5)	14 (31.1)	
Other	2 (4.2)	2 (4.4)	
Tobacco use	13 (32.5)	9 (22.5)	0.32
Median gestational age (days)	175.5 (162–181)	171 (161–181)	0.51[a]
Median interval between ultrasound and delivery (days)	3 (0–7)	2.5 (0–7)	0.59[a]

Note: Data are presented as *n* (%) and as mean (standard deviation) or median (minimum–maximum range).
[a]Mann–Whitney *U* test.
[b]χ^2 test or Fisher's exact test.

Table 2 Standard biometric parameters and intubation attempts

	One intubation attempt	More than one intubation attempt	*p*-Value	OR (95% CI)
Head circumference (mm)	216.9 (13.5)	214.6 (14)	0.99	1 (0.93–1.08)
Abdominal circumference (mm)	197.9 (17.1)	193.4 (16.2)	0.41	0.97 (0.90–1.04)
Biparietal diameter (mm)	58.7 (4.1)	58.1 (4)	0.97	1 (0.80–1.24)
Estimated fetal weight (grams)	688 (138.3)	657.7 (143.3)	0.74	1 (0.99–1.01)

Abbreviations: CI, confidence interval; OR, odds ratio.
Note: Data are presented as mean (standard deviation) using Mann–Whitney *U* test.

Table 3 Head circumference and intubation attempts based on gestational age

	One intubation attempt	More than one intubation attempt	*p*-Value
Head circumference			
23 wk' gestation	206.3 (6.3)	205.6 (4.5)	0.78
24 wk' gestation	211.7 (10.3)	210.8 (12.7)	0.86
25 wk' gestation	223.9 (13.2)	223 (14.6)	0.83
Head circumference $\leq$ 25th percentile			
23 wk' gestation	4 (40)[a]	5 (45.5)[a]	1[b]
24 wk' gestation	10 (76.9)[a]	9 (64.3)[a]	0.68[b]
25 wk' gestation	17 (70.8)[a]	11 (61.1)[a]	0.51
Head circumference $\leq$ 10th percentile			
23 wk' gestation	4 (40)[a]	5 (45.5)[a]	1
24 wk' gestation	10 (76.9)[a]	9 (64.3)[a]	0.68[b]
25 wk' gestation	17 (70.8)[a]	11 (61.1)[a]	0.51

Note: Data are presented as mean (standard deviation) or *n* (%).
[a]Student's *t*-test.
[b]χ^2 test or Fisher's exact test.

Table 4 Neonatal outcomes and intubation attempts

	One intubation attempt	More than one intubation attempt	*p*-Value	OR (95% CI)
Mean neonatal birth weight (grams)	711.8 (149.3)	699 (154.4)	0.68	
Neonatal death	8 (16.7)	13 (28.9)	0.16	2.03 (0.75–5.50)
Grade 3 or 4 IVH	7 (15.6)	9 (24.3)	0.32	1.74 (0.58–5.25)
Necrotizing enterocolitis	5 (11.4)	9 (24.3)	0.12	2.5 (0.75–8.30)
Periventricular leukomalacia	1 (2.3)	2 (5.6)	0.59[a]	2.47 (0.22–28.42)
Chest compressions	8 (16.7)	12 (26.7)	0.24	1.82 (0.67–4.97)
Epinephrine	3 (6.3)	13 (28.9)	0.004	6.09 (1.60–23.15)
Bronchopulmonary dysplasia	39 (90.7)	31 (86.1)	0.52	0.64 (0.15–2.57)
Median length of NICU admission (days)	104 (0–223)	104 (0–240)	0.44	

Abbreviations: CI, confidence interval; IVH, intraventricular hemorrhage; NICU, neonatal intensive care unit; OR, odds ratio.
Note: Data are presented as *n* (%) or as mean (standard deviation) or median (minimum–maximum range).
[a]χ^2 test or Fisher's exact test.

Although our study was not powered to detect a difference in neonatal outcome, we did observe an increasing trend toward more adverse neonatal outcome, specifically neonatal death, grade 3/4 interventricular hemorrhage, necrotizing enterocolitis, and periventricular leukomalacia, with increasing number of intubations that did not reach statistical significance. This is consistent with existing evidence that more than one intubation attempt is associated with neonatal death and neurodevelopmental impairment.[8]

This study is limited by its design. The retrospective nature of the data not collected for specific research purposes limits broad conclusions. For example, the experience level of the provider performing the intubation was not recorded consistently, and there is evidence that more experience is associated with more successful intubations.[12] Furthermore, specific counseling regarding provider experience is also unknown as it was not routinely documented. Time spent during resuscitation, not recorded in the dataset, may affect outcome. This study is also limited by the interval between biometric measurements and delivery. Although 7 days was chosen to minimize this inaccuracy, the HC increases by approximately 10 mm per week in the periviable period, and thus the differences in measurements between the time of the ultrasound and delivery could still affect its predictive value.

This study does not support the use of standard fetal biometric parameters for the prediction of difficult intubation in periviable neonates. At this time, antenatal counseling regarding intubation success should not be altered based on

individual fetal biometric measurements. It is not clear if alternative measurements that are not included in the standard biometric assessment would have an association with periviable intubation difficulty. Unfortunately, the prognosis for infants delivered in the periviable period remains guarded, and we have a limited ability to predict survival for any individual infant. Prospective studies are unlikely to be performed because periviable delivery is a rare obstetric complication. However, as the threshold of viability continues to change with the improvement of neonatal outcomes, more information on antenatal factors that can be used for outcome counseling is needed.

Authors' Contributions

Dr. Tara A. Lynch and Dr. Kathryn Drennan contributed to design, planning, conduct, data analysis, and manuscript writing. Dr. J. Christopher Glantz contributed to data analysis and manuscript writing.

Conflict of Interest

None.

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