ARTICLE

Impact of multiple intubation attempts on adverse tracheal intubation associated events in neonates: a report from the NEAR4NEOS

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OBJECTIVE: To determine the relationship between number of attempts and adverse events during neonatal intubation.
STUDY DESIGN: A retrospective study of prospectively collected data of intubations in the delivery room and NICU from the National Emergency Airway Registry for Neonates (NEAR4NEOS) in 17 academic centers from 1/2016 to 12/2019. We examined the association between tracheal intubation attempts [1, 2, and ≥3 (multiple attempts)] and clinical adverse outcomes (any tracheal intubation associated events (TIAE), severe TIAE, and severe oxygen desaturation).
RESULTS: Of 7708 intubations, 1474 (22%) required ≥3 attempts. Patient, provider, and practice factors were associated with higher TI attempts. Increasing intubation attempts was independently associated with a higher risk for TIAE. The adjusted odds ratio for TIAE and severe oxygen desaturation were significantly higher in TIs with 2 and ≥3 attempts than with one attempt.
CONCLUSION: The risk of adverse safety events during intubation increases with the number of intubation attempts.

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INTRODUCTION

Neonates are at high risk for adverse events associated with tracheal intubation (TI) [1–5]. Not only is the TI procedure technically challenging in neonates because of the unique airway anatomy [6, 7], but their structural and physiologic immaturity also makes them more vulnerable. The physiologic changes associated with intubation procedures, such as hypoxia- or vagal-induced bradycardia, hypertension, and increased intracranial blood pressure, can have detrimental effects on the immature developing neonatal brain[7–10]. Prolonged or repeated intubation attempts further exacerbate these physiologic derangements causing hemodynamic instability and cardiopulmonary decompensation, sometimes leading to death [3, 11–13].

Increased risk of tracheal intubation associated events (TIAEs) with the increasing number of intubations have been reported in adults and children [12–18]. The National Emergency Airway Registry for Children (NEAR4KIDS), an international airway registry of PICU (Pediatric intensive care unit) intubations, reported an independent effect on the number of attempts on non-severe TIAEs (e.g., esophageal intubation, main stem bronchial intubation, dysrhythmia, trauma), severe TIAEs (e.g., cardiac arrest, esophageal intubation with delayed recognition, emesis with aspiration, laryngospasm, hypotension) and oxygen desaturation in critically ill children [19]. Another airway registry for Emergency Department (ED) intubations from South Korea reported an increased incidence of adverse events with more than one attempt at intubation (11% vs. 5.8%) in pediatric patients [17]. A

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few studies suggested an increased risk of intraventricular hemorrhage (IVH) and neurodevelopment impairment with multiple intubation attempts in preterm infants [20, 21]. To date, the impact of multiple intubation attempts on safety outcomes in neonates has not been comprehensively evaluated.

The objective of our study was to evaluate the impact of the number of attempts on any TIAE, severe TIAE, and oxygen desaturations in neonates, accounting for patient, provider, and practice variables. We hypothesized that the number of intubation attempts would be associated with a higher risk of TIAEs in neonates.

METHODS

This study was a retrospective analysis of prospectively collected data from 17 academic Neonatal Intensive Care Units (14 from North America, one each from Singapore, Australia, and Germany) in the National Emergency Airway Registry for Neonates (NEAR4NEOS) between Jan 2016 and Dec 2019. Institutional review board approval or exemption as a quality improvement initiative was obtained at each participating center.

Data collection

A standardized tool was used to collect patient, practice, provider, and outcome data on all neonatal TIs performed at the participating NICUs. Each center was responsible for staff training to collect and verify the data and ensure compliance with the capture of >90% intubations. Each site obtained a specific compliance plan approval from the NEAR4NEOS Compliance Officer [1]. The site research coordinator was responsible for entering the verified data into a password-protected secure Research Electronic Data Capture system hosted by the Data Coordinating Centre at the Children's Hospital of Philadelphia.

We collected patient-related data, including the gestational age and weight (at birth and on the day of TI); provider-related data, including their training level and profession; and practice-related data, including the method of intubation (conventional laryngoscopy or video laryngoscopy), and premedication (sedative with the paralytic, sedative only, or no premedication). Outcome data on TIAEs (categorized as non-severe and severe TIAEs) and severe oxygen desaturation (≥20% decrease in SpO_2 from the highest level achieved before TI) were also collected.

Data definitions

Standard operational definitions previously described in the NEAR4NEOS registry were used for data collection and recording [1]. An encounter was defined as an episode of airway management until successful intubation. A course was defined as one method for the intubation, including the device, approach (nasal or oral), and premedication. An attempt was defined as an airway maneuver beginning with the insertion of the laryngoscope blade (conventional or video) into the patient's mouth and ending with its removal. There could be multiple attempts by different providers within a given course if all the attempts used the same method (i.e., the same airway device, approach, and medication). We assigned a new course to the encounter if any of the variables (device, approach, or medication) were altered with subsequent intubation attempt(s). The first course of the intubation encounter was utilized for this analysis.

Successful intubation was defined as endotracheal tube placement in the trachea, confirmed by chest rise, auscultation, second independent laryngoscopy, carbon dioxide (CO_2) detection, or chest radiograph. We defined *course success* as successful intubation by any provider, on any attempt, within that course.

We defined multiple attempts as intubations requiring more than two attempts (≥3) by the same or different providers for the successful placement of the endotracheal tube in the initial course.

Inclusion criteria

We included all intubation encounters performed in the Delivery Room (DR) and NICU from January 2016 to December 2019. We excluded intubations performed outside the DR and NICU (e.g., operating room, transport), intubations performed by non-NICU personnel (such as anesthesiologists and otorhinolaryngologists), and intubation for replacement of an existing tube.

Study outcomes

We categorized the adverse TIAEs as:

1. Non-severe TIAEs: esophageal intubation with immediate recognition, dysrhythmia including any duration of heart rate <60 beats per minute without chest compressions, main-stem bronchial intubation, emesis without aspiration, pain or agitation requiring additional medications causing a delay in intubation, epistaxis, lip trauma, medication error, and hypertension; and
2. Severe TIAEs: Cardiac arrest requiring chest compression for ≥1 min (died and survived), cardiac compressions <1 min, esophageal intubation with delayed recognition, emesis with aspiration, hypotension requiring therapy, laryngospasm, pneumothorax or pneumo-mediastinum, direct airway injury.

We collected data on oxygen desaturations separately from the adverse TIAEs, which included the highest oxygen saturation (SpO_2) immediately before the first intubation attempt and the lowest SpO_2 during the intubation course. We defined severe oxygen desaturations as ≥20% decrease in oxygen saturation from the highest level immediately before the first attempt [1].

Statistical analysis

Summary statistics to describe patient, provider, and practice characteristics were presented as frequencies for categorical variables, mean with standard deviation for normally distributed continuous variables, and median with interquartile ranges (IQR) for nonparametric variables. We described the relationship between patient, provider, and practice characteristic of the intubations with the number of intubation attempts using univariate analysis with Chi-square or Fisher's exact test for categorical variables and Wilcoxon rank-sum test for nonparametric variables. The number of intubation attempts was a priori categorized as one, two, and ≥3 (multiple) attempts [19]. We performed multivariate logistic regression analysis to evaluate the independent effect of the number of TI attempts on the outcomes (any TIAE, severe TIAEs, and severe oxygen desaturations). We adjusted for gestational age at birth (≤30 weeks, 31–35 weeks, and >35 weeks), weight at intubation (<1000 grams, 1000–2000 grams, and >2000 grams), location of intubation (DR vs. NICU), premedication (no sedation or paralytic, sedation only, sedation with paralytic), device used (conventional vs. video laryngoscopy) and any difficult airway feature on the exam [6]. We used the first attempt success as a reference. A p-value <0.05 was considered statistically significant. Stata version 15.1 (College Station, Texas, USA) was used for the analyses.

RESULTS

Of 7708 encounters, 6620 intubation encounters from 17 institutions were eligible for analysis. (Fig. 1) The median gestational age of the neonates at birth was 28 weeks, and the median (interquartile range) patient weight at intubation was 1611 (925, 2900) grams. Twenty-seven percent of intubations occurred in the DR and 73% in the NICU. Of the eligible TIs, 3449 (52%) were successful in the first attempt, 1697 (26%) on the second attempt, and 1474 (22%) required ≥3 attempts.

Table 1 summarizes the patient characteristics and their association with the number of TI attempts. The gestational age at birth and weight at intubation was lower among infants with ≥3 attempts than infants with successful intubation with one or two attempts ($p < 0.001$). Among the co-morbidities evaluated, acute respiratory failure was more frequently present in the encounters with ≥3 attempts. Surfactant administration, ventilation failure, oxygenation failure, and frequent apnea with bradycardia & desaturations were more commonly chosen as the indication for intubation in those with ≥3 attempts.

Provider and practice characteristics were significantly associated with the number of TI attempts, as shown in Table 2. First attempt success was proportionally higher for fellows and nurse practitioners. The pediatric residents as the first attempt provider had higher TIs with ≥3 attempts (27%) compared to TIs with 1 attempt (10%) and TIs with 2 attempts (18%). The conventional laryngoscope use was significantly more common in the TIs with

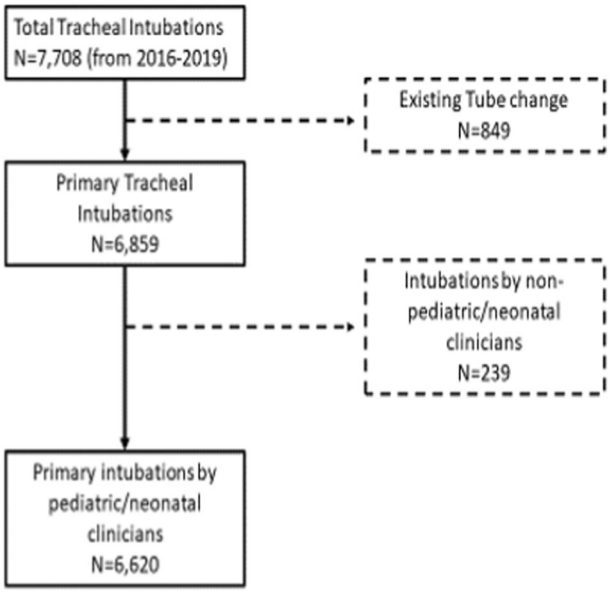

Fig. 1 Study enrollment.

≥3 attempts (84%) compared to the TIs with 1 (70%) or 2 attempts (76%), $p = 0.001$. Sedation and paralytic use were significantly less common in the ≥3 attempts (31%) compared to intubations with 1 (48%) or 2 attempts (38%), $p = 0.001$.

Tracheal Intubation safety outcomes

Adverse TIAE was reported in 1360 (20.5%) intubations; 293 (4.4%) were severe TIAEs. Severe oxygen desaturation was reported in 2778 (42%) intubations. The frequency of TIAEs and severe oxygen desaturations incrementally increased with the number of attempts (Fig. 2). Esophageal intubation with immediate recognition and dysrhythmia (including bradycardia <60bpm) were the most frequent non-severe TIAEs, and esophageal intubation with delayed recognition and gum trauma were the most frequent severe TIAEs. (Table 3).

In the multivariable analyses model accounting for patient (gestational age category, weight category at intubation, and any difficult airway feature) and practice characteristics (location, intubation device, and premedication), the odds for any TIAEs were significantly higher in TIs with 2 attempts (adjusted OR 5.00, 95% CI 4.20–5.94, $p < 0.001$) and TIs with ≥3 attempts (aOR 9.50, 95% CI 8.00–11.28, $p < 0.001$) compared to TIs with one attempt. (Tables 4 and 5) Similarly, the odds for severe TIAE and severe

Table 1. Patient characteristics categorized by number of intubation attempts.

Patient characteristics	1 attempt ($n = 3449$)	2 attempts ($n = 1697$)	≥3 attempts ($n = 1474$)	p value
Gestational age (weeks), median (IQR)	29 (25–36)	28 (25–35)	28 (25–33)	0.0001
≤30 weeks	1909 (55%)	1028 (61%)	990 (67%)	<0.001
31–35 weeks	629 (18%)	295 (17%)	240 (16%)	
≥36 weeks	910 (26%)	372 (26%)	244 (17%)	
Age at intubation (days), median (IQR)	1 (0–26)	1 (0–20)	2 (0–19)	0.0042
Weight at intubation (gram), median (IQR)[a]	1750 (970–3 000)	1460 (870–2 748)	1250 (800–2 400)	0.0001
≤1000 gm	963 (28%)	575 (34%)	576 (39%)	<0.001
1001–2000 gm	936 (27%)	469 (28%)	439 (30%)	
>2000 gm	1543 (45%)	648 (38%)	458 (31%)	
Sex (male, *n*, %)	2007 (58%)	975 (57%)	800 (54%)	0.046
Comorbidities, *n* (%)[b]				
Acute respiratory failure	2136 (62%)	1128 (66%)	1072 (73%)	<0.001
Chronic respiratory failure	553 (16%)	241 (14%)	226 (15%)	0.230
Congenital anomaly requiring surgery	349 (10%)	145 (9%)	81 (6%)	<0.001
Surgery/procedure for acquired disorder	178 (5%)	60 (4%)	61 (4%)	0.022
Congenital heart disease	239 (7%)	115 (7%)	62 (4%)	0.001
Airway or craniofacial anomaly	127 (4%)	61 (4%)	55 (4%)	0.978
Neurologic impairment	226 (7%)	94 (6%)	62 (4%)	0.005
Sepsis	166 (5%)	78 (5%)	69 (5%)	0.938
Indication, *n* (%)[b]				
Ventilation failure	955 (28%)	445 (26%)	434 (29%)	0.130
Oxygenation failure	1004 (29%)	473 (28%)	426 (29%)	0.647
Frequent apnea & bradycardia or desaturations	543 (16%)	267 (16%)	267 (18%)	0.094
Surfactant administration	723 (21%)	481 (28%)	465 (32%)	<0.001
Procedure	282 (8%)	113 (7%)	103 (7%)	0.103
Upper airway obstruction	116 (3%)	53 (3%)	44 (3%)	0.764
Unstable hemodynamics	105 (3%)	44 (3%)	30 (2%)	0.128
Delivery room, routine practice	111 (3%)	46 (3%)	27 (2%)	0.025
Delivery room, clinical indication	666 (19%)	418 (25%)	297 (20%)	<0.001
Unplanned extubation	363 (11%)	140 (8%)	77 (5%)	<0.001
Difficult Airway, *n* (%)				
History of difficult airway	247 (7%)	119 (7%)	107 (7%)	0.963
Any difficult airway feature	790 (23%)	380 (22%)	373 (25%)	0.111

IQR Interquartile range.
[a]Weight is missing in 13 patients.
[b]More than one comorbidity and indication could be selected for a given encounter.

Table 2. Provider and practice characteristics categorized by number of intubation attempts.

Provider and practice characteristics	1 attempt ($n = 3449$)	2 attempts ($n = 1697$)	≥3 attempts ($n = 1474$)	*p* value
First attempt provider[a]				<0.001
Neonatology Attending	336 (10%)	91 (5%)	38 (3%)	
Neonatology Fellow	1323 (38%)	607 (36%)	444 (30%)	
Pediatric Resident	361 (10%)	307 (18%)	395 (27%)	
Nurse practitioner	765 (22%)	397 (23%)	345 (23%)	
Physician Assistant	308 (9%)	143 (8%)	122 (8%)	
Hospitalist	74 (2%)	32 (2%)	41 (3%)	
Respiratory Therapist	254 (7%)	105 (6%)	73 (5%)	
Other	28 (1%)	11(1%)	16 (1%)	
Location				<0.001
DR	891 (26%)	514 (30%)	361 (24%)	
NICU	2558 (74%)	1183 (70%)	1113 (76%)	
Device[b]				<0.001
Conventional Laryngoscope	2404 (70%)	1295 (76%)	1236 (84%)	
Video Laryngoscope	1,034 (30%)	401 (24%)	232 (16%)	
Other	6 (0%)	0 (0%)	2 (0%)	
Premedication[c]				<0.001
Sedation with paralytic	1671 (48%)	639 (38%)	450 (31%)	
Sedative only	298 (9%)	203 (12%)	302 (20%)	
No sedative or paralytic	1,466 (43%)	849 (50%)	718 (49%)	

DR Delivery room, *NICU* Neonatal Intensive Care Unit.
[a]Provider information is missing in 4 intubations.
[b]Device information was missing for 12 intubations.
[c]24 intubation encounters reported paralysis only.

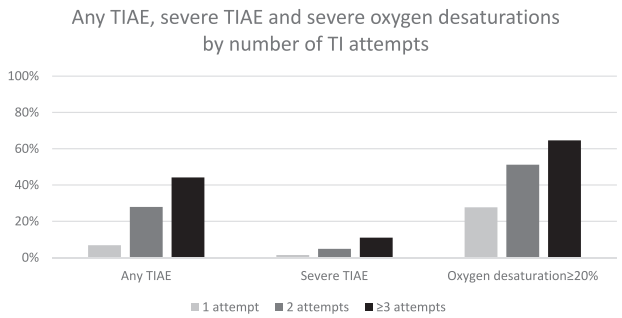

Fig. 2 Number of intubation attempts and outcome. Frequency of any TIAE, severe TIAE and severe oxygen desaturations incrementally increases with number of intubation attempts.

oxygen desaturation were significantly higher in TIs with 2 attempts and TIs with ≥3 attempts. (Table 4 and supplemental tables) Stratified analyses by the location of intubation (NICU, DR) demonstrated similar results.

DISCUSSION

This multicenter observational study evaluated the impact of the number of intubation attempts on adverse TIAEs and severe oxygen desaturation in neonates. We demonstrated that multiple (≥3) attempts needed for successful intubation are frequent in neonates (22%), and the frequency of TIAE and severe oxygen desaturation substantially increase with the number of attempts. There was an almost 10-fold increase in the adjusted odds for any TIAE, an 8-fold increase in the adjusted odds for severe TIAE, and a 6-fold increase in the adjusted odds of severe oxygen desaturations with multiple attempts (≥3) compared to first attempt success. Patient (gestational age at birth), provider (level of experience), and practice- related factors (device and premedication use) were associated with multiple attempts at intubation.

Neonates are inherently at higher risk for adverse TIAE because of their unique airway anatomy and vulnerability to physiologic derangements associated with the intubation procedure. Two small retrospective studies in extremely preterm infants show an association between multiple intubation attempts and the risk of severe IVH, death, and impaired neurodevelopment outcome [20, 21]. The evidence is otherwise sparse on intubation attempts and their effect on short-term (desaturations and TIAEs) and long-term (IVH and neurodevelopment) outcomes in neonates. Our study is the first large multicenter prospective study to report the incidence of multiple attempts for successful intubation in neonates and its impact on short-term procedural outcomes (i.e., adverse TAIEs and severe oxygen desaturations).

The number of attempts at intubation has been associated with the increased risk of adverse events in both adult and pediatric studies. A study of 2833 critically ill adults requiring emergent intubation outside of the operating room reported a 7-fold increase in the risk of cardiac arrest and a 14-fold increase in severe hypoxemia with multiple attempts (≥3) compared to those with ≤2 attempts [15]. Many single-center studies in children have also reported multiple TI attempts to be an independent risk factor for complications [16, 22, 23]. A large multicenter prospective study of critically ill children requiring intubation for acute respiratory failure showed a 5-fold increase in severe oxygen desaturation and a 2-fold increase in severe TIAE with ≥3 attempts compared to one attempt [19]. Similar to these adult and pediatric studies, our study found multiple attempts at intubation to be associated with an increased risk of adverse TIAEs in neonates. The incidence of multiple attempts (≥3) for successful intubation in neonates (22%) observed in our study is much higher compared to the incidence reported in

Table 3. Adverse tracheal intubation associated events (TIAE) by number of attempts.

Tracheal intubation associated events (TIAE)	1 attempt ($n = 3449$)	2 attempts ($n = 1697$)	≥3 attempts ($n = 1474$)	*p* value
Any TIAEs	235 (6.8%)	474 (27.9%)	651 (44.2%)	<0.001
Severe TIAEs	49 (1.4%)	82 (4.8%)	162 (11.0%)	<0.001
Cardiac arrest (died)	3 (0.1%)	1 (0.1%)	7 (0.5%)	
Cardiac arrest (survived)	12 (0.4%)	10 (0.6%)	5 (0.3%)	
Esophageal intubation with delayed recognition	1 (0.0%)	21 (1.2%)	50 (3.4%)	
Emesis with aspiration	6 (0.2%)	10 (0.6%)	3 (0.2%)	
Hypotension requiring therapy	2 (0.1%)	3 (0.2%)	2 (0.1%)	
Cardiac compressions <1 min	14 (0.4%)	12 (0.7%)	21 (1.4%)	
Laryngospasm	0 (0.0%)	6 (0.4%)	13 (0.9%)	
Pneumothorax or pneumo-mediastinum	2 (0.05%)	6 (0.3%)	10 (0.7%)	
Direct airway injury	2 (0.1%)	8 (0.5%)	21 (1.4%)	
Gum trauma	12 (0.4%)	15 (0.9%)	51 (3.5%)	
Non-severe TIAEs	200 (5.8%)	423 (24.9%)	577 (39.2%)	<0.001
Esophageal intubation with immediate recognition	16 (0.5%)	250 (14.7%)	390 (26.5%)	
Dysrhythmia	125 (3.6%)	134 (7.9%)	186 (12.6%)	
Main-stem bronchial intubation	39 (1.1%)	26 (1.5%)	52 (3.5%)	
Emesis without aspiration	8 (0.2%)	15 (0.9%)	15 (1.0%)	
Pain or agitation requiring additional medication	6 (0.2%)	15 (0.9%)	18 (1.2%)	
Epistaxis	2 (0.1%)	8 (0.5%)	0	
Lip trauma	10 (0.3%)	11 (0.7%)	11 (0.8%)	
Medication error	1 (0.0%)	0	1 (0.1%)	
Hypertension	1 (0.0%)	0	0	

Table 4. Multivariable analysis of TIAE, severe TIAE and oxygen desaturation by number of intubation attempts.

	1 attempt	2 attempts aOR* (95% CI) *p* value	≥3 attempts aOR* (95% CI) *p* value
Any TIAE	1 (reference)	5.00 (4.20, 5.94), <0.001	9.50 (8.00, 11.28), <0.001
Severe TIAE	1 (reference)	3.36 (2.34, 4.84), <0.001	7.57 (5.42, 10.58), <0.001
Oxygen desaturation ≥20%	1 (reference)	3.45 (3.02, 3.94), <0.001	5.87 (5.06, 6.80), <0.001

**aOR* Odds ratio adjusted for gestational age category at birth (≤30 week, 31–35 weeks, >35 weeks), weight at intubation (<1000 gm, 1000–2000 gm, >2000 gm), location of intubation (NICU vs DR), device (conventional vs video laryngoscope), premedication (no sedation or paralytic, sedation only, sedation and paralytic) and any difficult airway feature. *CI* confidence interval.

adults (8–11%) and children (9–15%) [13, 15, 19, 24]. The adjusted odds of adverse TIAE and severe oxygen desaturation with multiple attempts were also higher in neonates than those reported in infants and children [19] using similar operational definitions for adverse events.

We observed multiple patient-, provider-, and practice-related factors significantly associated with the number of TI attempts in neonates. Multiple attempts at intubation were higher in small and more premature infants, intubations for acute respiratory failure or surfactant administration, and with learners (fellows and residents) as the first attempt provider. On the other hand, the use of video laryngoscope and premedication (sedation with paralytic) were associated with a lower rate of multiple attempts. Prior studies on difficult intubation (≥3 attempts for successful intubation) in neonates and pediatric patients have reported results similar to our study [6, 13, 24, 25].

Out finding shows that more than one risk factors often affect the risk of multiple TI attempts; some are predictable and others modifiable. While patient-related factors are non-modifiable, we observed many modifiable factors (use of video laryngoscope, premedication, and provider training level) associated with reduced attempts for successful intubation, which could be used to mitigate the risk of multiple TI attempts [26–31].

Our study findings have important clinical implications in improving patient safety and outcome. First, identifying patient-related factors associated with multiple intubation and risk for TIAE could help in risk stratification. Infants of lower gestational age, lower weight at intubation, and those with underlying co-morbidities such as acute respiratory failure or congenital anomalies are inherently at higher risk for TIAE. We noted lower first-attempt success and a higher rate of multiple attempts among the residents as the first attempt provider. Thus, choosing a more experienced provider to attempt intubation of extremely preterm infants may minimize the number of attempts and TIAEs in the most vulnerable neonatal population. We also observed practice-related factors such as type of laryngoscope and premedication to be significantly associated with the number of attempts and TIAEs. Adopting video laryngoscope for intubations and optimizing the intubation condition with premedication (paralytic with sedatives) may improve first attempt success, especially for the novice intubators [28, 32, 33]. In our study, only 30% of intubations used video laryngoscope, and 48% used

Table 5. Multivariable analysis: Association of the number of attempts and Any TIAE.

	Odds ratio	95% CI	*p* value
Intubation attempts			
1 attempt	1 (reference)		
2 attempts	5.00	4.20–5.94	<0.001
≥3 attempts	9.50	8.00–11.28	<0.001
Location			
NICU	1 (reference)		
DR	0.86	0.72–1.02	0.089
Gestational age (weeks)			
≤30	1 (reference)		
31–35	0.74	0.60–0.93	0.008
≥36	0.66	0.52–0.86	0.001
Weight at intubation (g)			
>1000	1 (reference)		
1001–2000	0.90	0.76–1.07	0.231
>2000	0.96	0.76–1.21	0.786
Difficult airway feature	1.08	0.93–1.26	0.306
Premedication			
No sedation or paralytic	1 (reference)		
Sedation only	0.93	0.75–1.14	0.471
Sedation and paralytic	0.61	0.51–0.73	<0.001
Device			
Conventional laryngoscopy	1 (reference)		
Video laryngoscopy	0.54	0.45–0.67	<0.001

CI Confidence Interval, *NICU* Neonatal ICU, *DR* Delivery Room.

paralytic with sedation for intubation, showing the potential for improvement in these practice variables.

The strength of our study is that it presents the results of a large number of neonatal intubations collected prospectively from multiple centers. In addition, our study used a standard operational definition for attempts and adverse TIAE, allowing comparison among centers and with a pediatric intubation cohort (NEAR4KIDS). We acknowledge the limitations of our study, many of them inherent to the observational study design. The self-reporting of the events also introduces the possibility of recall bias. We analyzed only the first course of intubation encounter in the study, which could underestimate the true incidence of multiple attempts. However, only a tiny proportion of the TI encounters had more than one course. Our study examined the immediate adverse outcomes of multiple tracheal intubation attempts identified at the time of the procedure and the not remote outcomes (such as airway edema, extubation failure, subglottic stenosis, duration of mechanical ventilation, IVH, neurodevelopmental impairment), which are perhaps more clinically relevant.

In conclusion, our study demonstrates that multiple intubation attempts are frequent in neonates, and adverse TIAEs and oxygen desaturation increase with the number of attempts. We observed multiple modifiable and non-modifiable factors related to the patient, provider, and intubation practice associated with the number of intubation attempts. Interventions directed towards the modifiable factors could improve outcomes by reducing the number of attempts required for successful intubation.

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AUTHOR CONTRIBUTIONS

NS conceptualized and designed the study, analyzed the data, drafted the initial manuscript, and reviewed and revised the manuscript. All authors except JS coordinated and supervised data collection. JS and AN performed statistical analyses. All authors participated in data collection in their respective sites, interpreted the data and critically reviewed and revised the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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COMPETING INTERESTS

The authors have no conflicts of interest to declare. JB and NS are the site principal investigator for aerosolized surfactant clinical trial phase 2b sponsored by Aerogen.

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