



A prospective cross-sectional observational study of the prevalence and risks for laryngospasm in paediatric patients in four government-funded hospitals in KwaZulu-Natal, South Africa.

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Abstract

Background:

Laryngospasm (LS) is a common paediatric anaesthetic respiratory adverse event associated with serious complications if not detected and treated timeously.

Methods:

A prospective observational cross-sectional study was conducted from 15 May to 4 August 2023 in four government-funded hospitals in KwaZulu-Natal, South Africa. The primary outcome measure was the prevalence of laryngospasm, and a further aim was to identify associated factors, using binary logistic regression analyses.

Results:

905 participants were recruited. Mean patient age was 4.2 (SD $\pm$ 3.7) years. Most children were ASA physical status I and II (77.7%), presenting for elective surgery. The commonest comorbidity was an 'airway anomaly' (12.8%), followed by current or recent upper respiratory tract infection (URTI) in 11.6% of patients. The prevalence of laryngospasm was 10.1% and most occurred at emergence (54.9%). And 69.2% of children with LS had desaturation $<91\%$. Risks independently associated with LS were age (2 to 5 years; adjusted odds ratio [aOR] 2.15, $p=0.026$), an URTI (aOR 2.58, $p=0.004$), absence of a specialist in theatre (aOR 11.67, $p<0.001$), inhalational induction (aOR 10.21, $p=0.004$) or co-induction (aOR 6.34, $p=0.020$), use of a supraglottic airway device (SGAD) (aOR 2.17, $p=0.022$), inadequate depth of anaesthesia (aOR 13.98, $p<0.001$), non-use of neuromuscular blocker (aOR 4.64, $p=0.010$), and airway (aOR 2.27, $p=0.031$) and urological surgeries (aOR 2.75, $p=0.013$). No children had a serious complication, although two children were admitted to high care.

Conclusion:

The prevalence of LS in this study was 10-fold higher than in high-income countries, and the presence of a specialist anaesthetist is protective, indicating the importance of training in the reduction of perioperative critical events in children.

Recommendations:

Anaesthetists should be aware of the independent risk associated with laryngospasm as identified in this study and ensure such children are managed by a specialist anaesthesiologist.

Keywords: laryngospasm, peri-operative respiratory adverse events, paediatric anaesthesia

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Introduction

Laryngospasm (LS) is the reflex closure of the glottis, resulting in partial or complete upper airway obstruction. It is one of the commonest perioperative respiratory adverse events (PRAE) in anaesthetised children. It may result in serious complications if not promptly recognised and treated.^{1, 2} LS is 2 to 3 fold more common in the paediatric compared to adult patients, with an incidence of 0.9% in high-income countries (HIC), increasing up to 3-fold in infants.^{3, 4} In low- and middle-income countries (LMIC) the incidence is higher, ranging from 3.5 to 7.3% in South Africa (a middle-income country [MIC]),^{5, 6} and up to 18.4% in low-income countries (LIC).⁷

Numerous factors have been identified as associated with the occurrence of LS including: *patient related factors* e.g. younger age, airway reactivity or upper respiratory tract infection, passive smoking exposure, airway abnormalities, gastroesophageal reflux disease and higher American Society of Anaesthesiologists (ASA) Physical Status;^{8, 9} *anaesthesia related* e.g. inhalational induction, inadequate depth of anaesthesia, secretions in the airway, airway device used,^{8, 10} multiple attempts at airway management and use of muscle relaxants;⁷ and *surgical factors* e.g., airway surgery especially adenotonsillectomy, and hypospadias surgery. The level of skill or experience of the anaesthetic provider plays a role as well, with the lowest incidence being reported in paediatric anaesthetists, and increasing in incidence and related complications in those with the least experience, or anaesthetic consultants who have not recently practised paediatric anaesthesia.^{2,8,9}

LS may be underreported either due to failure of recognition or when prompt recognition and treatment of the laryngospasm occurred with no complications. We hypothesized the true prevalence of LS to be higher than previous South African studies, as these focused on multiple outcomes.^{5, 6} Identification of high-risk cases may improve patient safety through improved anticipation and vigilance, or referral to higher levels of care and directed quality improvement interventions.⁴ The objective of this study was to determine the prevalence of LS and associated factors in children aged 12 years and under, presenting for a general anaesthetic at four urban hospitals in KwaZulu-Natal, South Africa.

Methods

Study design, setting, and participants

A prospective observational cross-sectional study was conducted from 15 May to 4 August 2023 in four government-funded hospitals in KwaZulu-Natal, South

Africa. Hospitals included a second-level (regional) hospital (Harry Gwala Regional Hospital), and three third-level hospitals, two tertiary and one quaternary/central hospital, namely, Grey's Hospital and Victoria Mxenge Hospital (formerly known as King Edward VIII Hospital) and Inkosi Albert Luthuli Central Hospital, respectively. Inclusion criteria were all children 12 years and under presenting for a surgical procedure and undergoing general anaesthesia during the study period. To avoid selection bias, investigators aimed to recruit all eligible consecutive patients into the study. Children already intubated or with a tracheostomy were excluded from the study.

Variables and data

A case record form (CRF) was designed for data collection. Variables describing the baseline characteristics of participants were collected and included the following; age, sex, ASA physical status and comorbidities, hospital level, type of surgery, urgency of the surgery, the level of seniority of the anaesthesiologist present in the operating room as well as operating the airway (i.e. placing the airway device), type of induction and maintenance, definitive airway device used, number of attempts and difficulties encountered, depth of anaesthesia and the use of neuromuscular blocking agents. Airway surgery was defined as a procedure occurring in the mouth and upper airway, also known as a shared airway, where both the surgeon and the anaesthetist required access to the airway. The primary outcome measure was the occurrence of laryngospasm as clinically diagnosed by the attending anaesthesiologist. LS was clinically defined as new onset stridor with limited ventilation or bag movement disproportionate to breathing efforts, or tracheal tug potentially progressing to silent chest movement with no bag movement or ventilation possible.^{11, 12} Timing of the LS episode (induction, maintenance phase, extubation/emergence, multiple), complications (bradycardia, desaturation, cardiac arrest and/or unplanned high care or Intensive Care Unit (ICU) admission) and management (use of suction, supplementary oxygen, jaw thrust, continuous positive airway pressure (CPAP), propofol, suxamethonium, reintubation, intravenous lignocaine, topical lignocaine¹⁶, and 'other') were recorded. Information from the CRF was entered into a password-protected database.

Study size

Based on the reported incidence of LS from previous South African studies,^{5, 6} we hypothesized a prevalence of 7.5%



and calculated a sample size of 107 to determine the prevalence of laryngospasm, for a precision of 5% with 95% confidence intervals.¹³ However, as we also sought to identify factors associated with LS, we estimated a sample size of 950 patients would allow us to test up to eight variables using the rule of thumb of 10 events per variable.¹⁴

Statistical methods

We reported the mean and standard deviation ($\pm$ SD) for age and then used a t-test to test for the difference in mean age between children with and without LS. Categorical variables are presented as frequency (percent), and differences were compared using χ^2 and Fisher's exact tests and then reported as appropriate. Univariable analysis was then performed to study the association between each variable and our primary outcome, LS, and reported these as unadjusted odds ratios (OR) and 95% confidence intervals (CI).

To assess the association between several exposure variables and the development of LS, we used logistic regression analysis, and results are presented as unadjusted univariable (OR) and multivariable adjusted odds ratios (aOR) and 95% CI. We decided to construct the model in two steps. We included 7 *a priori* variables based on risks reported in the literature: i) age of patient; ii) airway surgery or shared airway; iii) years of experience of the anaesthetist (specialist vs non specialist); iv) acute recent upper respiratory tract infection (URTI) within the past 4 weeks; v) type of induction (inhalational vs intravenous); vi) type of airway device used (endotracheal tube [ETT] vs supraglottic airway device [SGAD]); and the vii) depth of anaesthesia at time of airway manipulation. Whilst many factors are listed in the literature, evidence for independent risk factors is lacking for many of the factors mentioned. Three further candidate variables were then entered into the

model based on their univariable performance (p value <0.05), and clinical utility, namely: viii) multiple attempts at securing the airway; ix) urological surgery (noting this has been mentioned in the literature); x) the presence of airway difficulties and xi) the use of a muscle relaxant for eleven total factors. Although this exceeded the 10 events per variable, we were still within acceptable limits for the number of events per variable.¹⁴ This would allow the exploration of candidate variables not initially anticipated or described in the literature. Factors were tested for collinearity, using the variance inflation factor (VIF). If collinearity was detected ($VIF > 2$), then variables would either be excluded or combined.

Statistical analyses were performed using SPSS Statistics version 29 (IBM). A P value of <0.05 was considered statistically significant for all analyses.

Ethical considerations

Ethical approval was sought in August 2022 and granted in May 2023 from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, South Africa (BREC/00004633/2022). A waiver of individual consent was approved. Hospital site and Department of Health permissions for data collection were sought and granted for each study site. Our findings are reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement¹⁵

Results

Recruitment and cohort characteristics

After excluding participants meeting the exclusion criteria and incomplete case record forms, 905 patients were recruited from 4 participating hospitals between May and August 2023 and were entered into the final database for analysis (Figure 1).

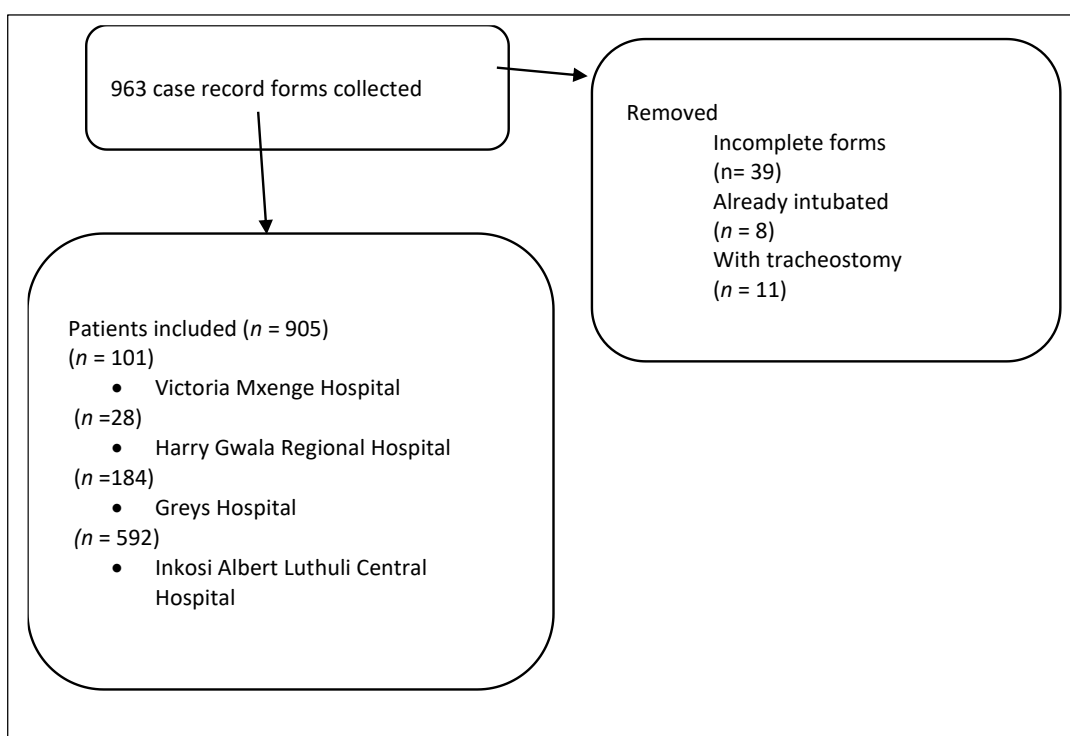


Figure 1: Patient selection flow diagram

The mean patient age was 4.2 (SD $\pm$ 3.7) years, and included 45 (5%) neonates, 307 (33.9%) infants (29 days to 1 year-old), 268 (29.6%) preschool children (2 – 5 years), and 285 (31.5%) school-aged children (6 – 12years). Most children were ASA physical status I and II (704 [77.7%]), presenting for elective surgery, during daytime hours (847 [93.6%]), and managed at a quaternary level of care 592 [65.4%].

Abdominal 242 (26.7%) surgeries were the most common, followed by airway surgery 174 (19.2%), which included ear, nose, and throat (ENT), dental, maxillofacial, and palatal surgeries. The most common comorbidity was an ‘airway anomaly’ in 116 (12.8%) patients, and current upper respiratory tract infection (URTI) in 105 (11.6%) patients (Table 1).

Table 1. Baseline characteristics of participants

Variable		All patients (n=905) N (%)	Patients with laryngospas m (n=91)	Patients without laryngospasm (n=814)	Univariate Ratio (95% CI) Odds	P value
Age	Mean ($\pm$ SD)	4.2 (3.7)	3.7 (3.2)	4.2 (3.7)	0.96 (0.91-1.02)	0.228
Age categories		n=905	91 (10.1%)	814 (89.9%)	Chi-squared p=0.042	
Neonates (0-28 d)		45 (5)	1 (2.2)	44 (97.8)	0.24 (0.03 – 1.87)	0.176
29d –1 y		307 (33.9)	29 (9.4)	278 (90.6)	1.13 (0.644 – 1.99)	0.663
2 – 5 y		268 (29.6)	37 (13.8)	231 (86.2)	1.74 (1.01 – 2.99)	0.045
6 –12 y		285 (31.5)	91 (10.1)	814 (89.9)	Reference	0.060
Sex		n=903			Chi-squared p=0.667	

Male	535 (59.2)	52 (9.7)	483 (90.3)	Reference	
Female	368 (40.7)	39 (10.6)	329 (89.4)	1.10 (0.71 – 1.70)	0.667
ASA physical status	n=904			Chi-squared p=0.032	
I	355 (39.3)	47 (13.2)	308 (86.8)	Reference	
II	349 (38.6)	30 (8.6)	319 (91.4)	0.616 (0.389 – 1.00)	0.050
III - V	200 (22.1)	14 (7.0)	186 (93.0)	0.493 (0.264 – 0.920)	0.026
Urgency of surgery	n=904			Chi-squared p= 0.871	
Elective	800 (88.5)	81 (10.1)	719 (89.9)	Reference	
Urgent/Emergent	104 (11.5)	10 (9.6)	94 (90.4)	0.944 (0.473 – 1.855)	0.871
Time of induction	904			Fischer's p=0.328	
Daytime	847 (93.6)	83 (9.8)	764 (90.2)	Reference	
Afterhours	58 (6.4)	8 (13.8)	50 (86.2)	1.493 (0.675 – 3.213)	0.331
Type of surgery				Chi-squared p=0.009	
Abdominal	242 (26.7)	14 (5.8)	228 (94.2)	Reference	
Airway surgery (shared airway)	174 (19.2)	21 (12.1)	153 (87.9)	2.235 (1.103 – 4.531)	0.026
Neurosurgery	110 (12.2)	7 (6.4)	103 (93.6)	1.107 (0.434 – 2.824)	0.832
Cardiac	20 (2.2)	0 (0.0)	20 (100.0)	0.000	N/A
Ophthalmology	76 (8.4)	12 (15.8)	64 (84.2)	3.054 (1.346 – 6.929)	0.008
Orthopaedics	137 (15.1)	19 (13.9)	118 (86.1)	2.622 (1.270 – 5.416)	0.009
Plastics + Burns	87 (9.2)	7 (8.0)	80 (92.2)	1.425 (0.555 – 3.657)	0.461
Urological	57 (6.3)	11 (19.3)	46 (80.7)	3.894 (1.663 – 9.119)	0.002
CVC	2 (0.2)	0 (0.0)	2 (100.0)	0.000	N/A
Comorbidities					
Airway anomaly	116 (12.8)	14 (12.1)	102 (87.9)	1.269 (0.692 – 2.327)	0.441
Asthma	3 (0.3)	0 (0)	3 (100)	–	–
Current URTI	105 (11.6)	21 (20.0)	84 (80.0)	2.607 (1.523 – 4.462)	<0.001
GORD	9 (1.0)	1 (11.1)	8 (88.9)	1.119 (0.138 – 9.053)	0.916
Passive smoking	2 (0.2)	0 (0)	2 (100)	–	–
Chronic respiratory condition	7 (0.8)	0 (0)	7 (100)	–	–
Sleep Apnoea	23 (2.5)	2 (8.7)	21 (91.3)	0.826 (0.196 – 3.679)	0.826
Congenital HD	23 (2.5)	1 (4.3)	22 (95.7)	0.400 (0.053 – 3.003)	0.373
Other	73 (8.1)	9 (12.3)	64 (87.7)	1.286 (0.617 – 2.680)	0.502
Syndrome	22 (2.4)	1 (4.5)	21 (95.7)	0.420 (0.056 – 3.156)	0.399
Hospital level	N=905			Chi-squared p=0.416	
Regional (1 hospital)	28 (3.1)	2 (7.1)	26 (92.9)	0.751 (0.174 – 3.249)	0.702
Tertiary (2 hospitals)	285 (31.5)	34 (11.9)	251 (88.1)	1.323 (0.841 – 2.081)	0.227
Quaternary (1 hospital)	592 (65.4)	55 (9.3)	537 (90.7)	Reference	0.419

Abbreviations: ASA=American Society of Anaesthesiologists; CI=confidence interval; URTI=upper respiratory tract infection; GORD=gastroesophageal reflux disease; CHD=congenital heart disease; SD=standard deviation.

Anaesthetic conduct

A specialist anaesthetist was the most senior anaesthesia provider in the operating room in 94.6% of cases; however, the most common primary airway operator was a medical

officer or registrar (resident) (74.9%), with a minimum of a Diploma in Anaesthesia (DA) Table 2. Most children 501, 55.4%) underwent a 'combined or co-induction' described by the attending anaesthesiologists as an inhalational

induction, rapidly followed by a bolus of propofol and or ketamine.¹⁴ The reasons stated in 98.6% were “routine practice” with the remaining 1.4% choosing this method to prevent laryngospasm. 300 children (33.1%) had an inhalational induction, 99% with sevoflurane, and only 104 (11.5%) had an intravenous induction. Maintenance of anaesthesia was via inhalational with sevoflurane in 94% of cases. An endotracheal tube was the most common

definitive airway device used, 569 (62.9%), followed by an SGAD used in 267 (29.5%) (Table 2).

It was noted that 108 (11.9%) patients had multiple attempts at airway device placement, and further airway difficulties (bag mask ventilation, laryngoscopy, or intubation) were encountered in 24 (2.7%) patients. Most children 726, 80.2%) did not have a neuromuscular blocker administered.

Table 2. Anaesthetic management of the cohort

Variable	All patients (n=905) N (%)	Patients with laryngospasm (n=91)	Patients without laryngospasm (n=814)	Univariate Odds Ratio (95% CI)	P value
Most senior anaesthetists present				Chi-squared p<0.001	
DA/Registrar	49 (5.4)	13 (26.5)	36 (73.5)	3.602 (1.833 – 7.078)	<0.001
Specialist	856 (94.6)	78 (9.1)	778 (90.9)	Reference	
Final airway operator (highest qualification)				Chi-squared p<0.001	
Pre-DA	102 (11.3)	10 (9.8)	92 (90.2)	0.422 (0.193 – 0.923)	0.031
DA/Registrar	676 (74.7)	55 (8.1)	621 (91.9)	0.344 (0.206 – 0.574)	<0.001
Specialist	127 (14.0)	26 (20.4)	101 (79.5)	Reference	
Type of induction				Chi-squared p=0.031	
Inhalational	300 (33.1)	35 (11.7)	265 (88.3)	4.447 (1.338 – 14.780)	0.015
Combined / co-induction	501 (55.4)	53 (10.6)	448 (89.4)	3.983 (1.220 – 13.001)	0.022
Intravenous	104 (11.5)	3 (2.9)	101 (97.1)	Reference	
Maintenance				Chi-squared p=0.888	
Inhalational	851 (94.0)	86 (10.1)	765 (89.9)	N/A	N/A
Combination	2 (0.2)	0 (0)	2 (100)	N/A	N/A
TIVA	52 (5.7)	5 (9.6)	47 (90.4)	N/A	N/A
Definitive airway				Chi-squared p=0.005	
Face mask	10 (1.1)	1 (10.0)	9 (90.0)	Reference	0.023
SGAD	267 (29.5)	36 (13.5)	231 (86.5)	1.403 (0.173 – 11.404)	0.752
ETT	569 (62.9)	48 (8.4)	521 (91.6)	0.829 (0.103 – 6.684)	0.860
SGAD converted to ETT	6 (0.7)	3 (50.0)	3 (50.0)	9.00 (0.660 – 122.794)	0.099
Tubeless	51 (5.6)	5 (5.9)	48 (94.1)	0.562 (0.052 – 6.032)	0.635
Rigid Bronchoscope	2 (0.2)	0 (0.0)	2 (100.0)	0.000	0.999
Definitive airway (SGAD compared to ETT)				Chi-squared p=0.024	
SGAD	267 (29.5)	36 (13.5)	231 (86.5)	1.692 (1.069 – 2.677)	0.025
ETT	569 (62.9)	48 (8.4)	521 (91.6)	Reference	
Attempts at airway device placement				Chi-squared <0.001	
None/Single	797 (88.1)	63 (7.9)	734 (92.1)	Reference	
Multiple	797 (88.1)	28 (25.9)	80 (74.1)	4.078 (2.470 – 6.733)	<0.001
Attempts compared					



None/One	797 (88.1)	63 (7.9)	735 (92.1)	Reference	<0.001
Two	70 (7.7)	15 (21.4)	55 (78.6)	3.177 (1.699 – 5.944)	<0.001
Three	30 (3.3)	10 (33.3)	20 (66.7)	5.825 (2.614 -12.984)	<0.001
Four or more	8 (0.9)	3 (37.5)	5 (62.5)	6.990 (1.633 – 29.930)	0.009
Depth of anaesthesia				Chi-squared <0.001	
Adequate	876 (97.1)	76 (8.6)	803 (91.4)	Reference	
Inadequate	26 (2.9)	15 (57.7)	11 (42.3)	14.408 (6.392–32.479)	<0.001
Airway difficulties	N=905			Chi-squared <0.001	
Nil	881 (97.3)	83 (9.4)	798 (90.6)	Reference	
Any	24 (2.7)	8 (33.3)	16 (66.7)	4.807 (2.997 – 11.570)	<0.001
Type of difficulty					
BMV	9 (1.0)	1 (11.1)	8 (88.9)	–	–
Laryngoscopy	11 (1.2)	5 (45.5)	6 (54.5)	–	–
Intubation	4 (0.4)	2 (50.0)	2 (50.0)	–	–
Neuromuscular blocker				Chi-squared <0.001	
Nil	726 (80.2)	79 (10.9)	647 (89.1)	Reference	
Depolarising	23 (2.5)	8 (34.8)	15 (65.2)	4.368 (1.795 – 10.629)	0.001
Non-depolarising	156 (17.2)	4 (2.6)	152 (97.4)	0.216 (0.078 -0.588)	0.003

Abbreviations: DA = Diploma in anaesthesia; TIVA = total intravenous anaesthesia; SGAD = supraglottic airway device; ETT = endotracheal tube; BMV = bag mask ventilation

Prevalence, timing, complications, and management of LS

91 patients had a laryngospasm episode documented, showing an overall prevalence of 10.1% (95% CI, 8.1–12.0) (Tables 1 and 3). The majority of LS occurred at

extubation/emergence 50, 54.9%), followed by 35 (38.5%) at induction (Table 3). The most common complication was desaturation to <91%, experienced by 63 (65%) of children with LS. Only 3 (3.3%) patients experienced bradycardia; there were no cardiac arrests, and 2 (2.4%) had an unplanned high care admission. No patients were admitted to the ICU.

Table 3. Prevalence, distribution, management, and outcomes of Laryngospasm

	n/N (%)		
Laryngospasm (LS)	91/905 (10.1)		
Timing			
Induction	35 (38.5)		
Intraoperatively	5 (5.5)		
Extubation/emergence	50 (54.9)		
Other/multiple	1 (1.1)		
Outcomes	No	Yes	Unknown
Bradycardia	87 (95.6)	3 (3.3)	1 (1.1)
Desaturation (<91%)	26 (28.6)	63 (69.2)	2 (2.2)
Cardiac arrest	91 (100.0)	0 (0)	0
High care	82 (97.6)	2 (2.4)	0
Lowest saturation (%) recorded in LS patients	n=74 had saturation recorded		
< 50	11 (14.9)		



51 to 80	26 (35.1)		
81 to 90	26 (35.1)		
>91	11 (14.9)		
Management	No	Yes	Unknown
Suction	46 (50.5)	42 (46.2)	3 (3.3)
Oxygen	33 (36.3)	55 (60.4)	3 (3.3)
Jaw Thrust	17 (18.7)	71 (78.0)	3 (3.3)
CPAP	21 (23.1)	69 (75.8)	1 (1.1)
Propofol	51 (56.0)	37 (40.7)	3 (3.3)
Suxamethonium	81 (89.0)	6 (4.4)	4 (4.4)
Reintubation	84 (92.3)	3 (3.3)	4 (4.4)
Intravenous Lignocaine	83 (91.2)	4 (4.4)	4 (4.4)
Topical lignocaine	85 (93.4)	2 (2.2)	4 (4.4)
Other	83 (91.2)	4 (4.4)	4 (4.4)
Other management	4 (4.4)		
Magnesium	1 (1.1)		
Naloxone	1 (1.1)		
Non-depolariser NMB	1 (1.1)		
Changed airway	1 (1.1)		

Abbreviations: LS=laryngospasm; CPAP=continuous positive airway pressure; NMB=neuromuscular blocker

Table 4. Multivariable analysis of factors associated with laryngospasm

Variable	n (%) (N=905)	Univariable analysis		Multivariable analysis	
		OR (95% CI)	P value	aOR (95% CI)	P value
Age					
Neonates (0-28 d)	45 (5)	0.24 (0.03 – 1.87)	0.176	0.38 (0.04 – 3.49)	0.391
29d –1 y	307 (33.9)	1.13 (0.644 – 1.99)	0.663	1.79 (0.86 – 3.73)	0.118
2 – 5 y	268 (29.6)	1.74 (1.01 – 2.99)	0.045	2.15 (1.10 – 4.20)	0.026
6 –12 y	285 (31.5)	Reference	0.060	Reference	0.076
Comorbidities					
Current URTI	105 (11.6)	2.61 (1.52 – 4.46)	<0.001	2.58 (1.34 – 4.94)	0.004
The most senior anaesthetist in the room					
DA/Registrar	49 (5.4)	3.60 (1.83 – 7.08)	<0.001	11.67 (5.10–26.86)	<0.001
Specialist	856 (94.6)	Reference		Reference	
Type of induction					
Inhalational	300 (33.1)	4.45 (1.34 – 14.78)	0.015	10.21 (2.10 – 49.91)	0.004
Combined / co-induction	501 (55.4)	3.98 (1.22 – 13.00)	0.022	6.34 (1.34 – 29.95)	0.020
Intravenous	104 (11.5)	Reference		Reference	
Airway device SGAD vs ETT					
SGAD	267 (29.5)	1.69 (1.07 – 2.67)	0.025	2.17 (1.12 – 4.22)	0.022
ETT	569 (62.9)	Reference		Reference	
Airway attempts					



Single attempt	797 (88.1)	Reference		Reference	
More than one /multiple	797 (88.1)	4.08 (2.47 – 6.73)	<0.001	3.47 (1.81 – 6.64)	<0.001
Depth of anaesthesia					
Adequate	876 (97.1)	Reference		Reference	
Inadequate	26 (2.9)	14.41 (6.39–32.48)	<0.001	13.98 (4.82 – 40.09)	<0.001
Other airway difficulties					
Nil	881 (97.3)	Reference		Reference	
Any	24 (2.7)	4.80 (2.30 – 11.57)	<0.001	2.62 (0.79 – 8.70)	0.115
Neuromuscular blocking agents					
Nil vs	726 (80.2)	4.64 (1.67– 12.87)	0.003	4.64 (1.45 – 14.90)	0.010
Depolarising	23 (2.5)	20.26 (5.46– 75.28)	<0.001	20.47 (3.23 – 129.94)	0.001
Non-depolarising	156 (17.2)	Reference		Reference	
AW surgery					
Shared airway (airway surgery)	174 (19.2)	2.24 (1.10 – 4.53)	0.026	2.27 (1.08 – 4.77)	0.031
Urological surgery	57 (6.3)	3.89 (1.66 – 9.12)	0.002	2.75 (1.23 – 6.12)	0.013

Abbreviations: OR= Odds Ratio; aOR=adjusted Odds Ratio; URTI= upper respiratory tract infection; SGAD=supraglottic airway device; ETT= endotracheal tube

Discussion

This prospective multi-centred cross-sectional observational study carried out in four hospitals in KwaZulu-Natal, South Africa, found that one in ten children had an episode of laryngospasm and identified that age (children 2 – 5 years), current or recent acute URTI, absence of a specialist in the theatre during anaesthetic induction or emergence, airway surgery (shared airway) and urological surgery, use of inhalational and co-induction techniques, multiple airway device placement attempts, use of a SGAD over an ETT, inadequate depth of anaesthesia when airway manipulation occurs, were independently associated with laryngospasm, whilst use of non-depolarising muscle relaxants was protective.

Prevalence

The overall prevalence of laryngospasm was 10.1%, almost twice that found in a previous multicentre South African study (3.4%) and slightly higher than the recent single centre South African study (7.3%).⁶ A plausible reason for this could be that the previous studies looked at all critical events occurring peri-operatively in the paediatric population and not just at laryngospasm in isolation; therefore, there was a possible underreporting of cases that the clinicians did not consider significant. The prevalence in this study was, however, almost half that found in Ethiopia (18.4%), in keeping with studies identifying higher critical incidents in LIC vs MIC, but is still tenfold higher than the overall prevalence of 0.9% found in HIC.³ This demonstrates the

impact of funding, resources, and training on the prevalence of paediatric perioperative critical incidents.

It should be noted that in our study, emergence was a high-risk period for the development of LS, indicating that continued vigilance is required in all phases of paediatric anaesthesia, not just at induction.

Risk factors

There are several risk factors described in the literature, and this study confirmed many of these but also highlighted some important new findings, namely the absence of a specialist in the theatre, the number of airway manipulation attempts, and a “co-induction technique” common in our practice.

Years of experience of the anaesthetist

Experience was defined as a consultant or specialist anaesthetist, as compared to a registrar (resident) or house officer, and compared the differences found when a consultant anaesthetist was present or absent in the operating room, and when a consultant anaesthetist was the final operator of the airway. In our univariable analysis, it was found that a specialist anaesthesiologist as the final airway operator had an increased risk of LS. This did not seem to be supported in the literature. It is postulated that this could be due to the consultant anaesthetist being the last provider to attempt airway instrumentation after attempts by the registrar or house officer, when airway issues had already occurred or that the patient was identified as a high-risk patient pre-op, or in this scenario due to the human nature of



becoming task focused, that the delegation of team lead automatically falls to the registrar or house officer as the consultant focuses on the airway, or a combination of the above factors.

This postulate is further supported by our study identifying the absence of a consultant in the theatre room as highly associated with the development of LS, with a 12-fold increase in risk (aOR 11.67, $p < 0.001$) compared to when a consultant anaesthetist was present in the room. The presence of a consultant anaesthetist in the room was protective of LS, and the postulate is that there may have been better decision-making regarding patient and airway management.

Depth of anaesthesia:

Manipulating the airway or the patient in lighter planes of anaesthesia carried a thirteen-fold independent risk of developing LS (aOR 13.98, $p < 0.01$), making it the factor with the highest odds for developing LS in our study, and reinforces the importance of ensuring adequate depth of anaesthesia before airway manipulation or instrumentation.

Type of induction:

Inhalational induction was found to be an independent risk factor with a 10-fold increase in the development of LS when used (aOR 10.21, $p = 0.004$), with an intravenous technique being protective. However, most of the anaesthetists from our study practised a combined or co-induction technique, described as an inhalational induction, followed by a rapid intravenous dose of propofol or ketamine, or a combination of propofol, opioid, and or ketamine.¹⁶ Interestingly, in this study, this technique carried an increased risk of LS (aOR 6.34, $p = 0.020$) when compared to sole intravenous induction. It is not completely possible to exclude the use of propofol in this group to treat LS as a contributory or confounding factor, as propofol was used in 37 patients to treat LS. The investigators, however, have reservations about the technique as far more patients received propofol as part of the co-induction, compared to those who received it as LS treatment – thus, there are still valid concerns about the technique potentially increasing risk for LS.

Presence of recent URTI:

105 (11.6%) of the study cohort had a recent URTI (current or within 4 weeks of the study), and 20% of these experienced LS. On multivariable analysis, recent URTI increased the risk of LS almost threefold (aOR 2.58;

$p = 0.004$). This is confirmed in the literature and ties in with the preschool age, as that is the age group most likely to present with a history of a recent URTI.

Patient's age:

Preschool children aged 2 – 5 years had a twofold higher prevalence of developing LS compared to the other age groups, and this age group was also shown to be an independent risk factor for the development of LS, with an aOR of 2.1 ($p = 0.026$). This has been widely confirmed in previous studies and is a known accepted fact in literature. Thus, preschool children must be managed with increased vigilance or specialist presence.

Airway device:

Most literature describes the use of a supraglottic device as protective over the use of an ETT, but in this study, 13.5% of the patients who developed LS had a SGAD, compared to 8.4% with an ETT, (aOR 2.17, $p = 0.022$), implying that the use of an ETT was protective over the use of SGAD, or that SGAD conferred twice the risk. This is possibly due to several postulated factors, like the use of a muscle relaxant with the ETT, or that most anaesthetists were more vigilant with anaesthetic depth before intubating, as compared to before the use of a SGAD. This contrasts with the Ethiopian study,⁷ where most of the patients who experienced LS were intubated patients.

Number of attempts at airway manipulation:

More than one attempt at airway device placement management resulted in a threefold increased risk of laryngospasm when compared with a single attempt (aOR 3.47, $p < 0.001$). The exact reasons for this were not explicitly stated by the attending anaesthetist, but it is interesting to note that the Ethiopian study⁷ also noted the same finding, with multiple airway attempts showing a 2.47-fold increased likelihood of laryngospasm when compared to a single attempt.

Use of muscle relaxant:

The use of a non-depolarising neuromuscular blocking agent (NMB) was a protective factor against the development of LS compared to no NMB, which increased risk four-fold (aOR 4.64, $p = 0.010$). This study further demonstrated that use of a depolarising NMB (Suxamethonium) was associated with a 20-fold increased risk of LS, although use of Suxamethonium to treat LS (in 6/23 patients that received Suxamethonium) may be a confounder to these results. The



protective effect of a non-depolarising NMB may have occurred because, with the use of a muscle relaxant, an adequate plane of anaesthesia to enable safe airway instrumentation was reached, whereas Suxamethonium was used as a rescue where LS had already occurred.

Surgical risks:

Airway surgery and urological surgery are described in the literature as risk factors for LS. Our study confirmed both to be independent associations, demonstrating a three-fold increase in LS in patients undergoing urological surgical procedures (aOR 2.75, $p=0.013$) and a two-fold increase (aOR 2.27, $p=0.031$) in airway surgery.

Treatment and outcomes

The most common adverse event associated with laryngospasm was desaturation, with 69.2% of the patients desaturating to an oxygen saturation of $<91\%$. The most common treatment methods employed to break the spasm included applying a jaw thrust (78%), CPAP (75.8%), supplemental oxygen (60.4%), the use of suction (46.2%), and the use of propofol (40.7%).

3.3% of patients required reintubation. Other modalities suggested in literature but not really used by attending anaesthetists in this study included administration of lignocaine (IV 4.4% and topical 2.2%), suxamethonium (4.4%), and IV magnesium (0.1%).¹⁷ This may be an area of education and quality improvement in the management of the units studied. None of the patients had a cardiac arrest or required ICU admission secondary to the LS, although two were admitted to high care for overnight observation.

Generalisability

Due to the large sample size and high-quality data collection, the findings of this study will likely be generalisable to similar hospital types, with a similar profile of children presenting for surgery. The frequent use of a “co-induction technique” in the units studied may reduce the generalisability to units that manage inductions differently. The high percentage of specialist anaesthetists present in theatre (94.6%) means that the findings of this study may not be generalisable to hospitals where children are not managed with a specialist present. However, the risks identified will be generalisable to all units conducting paediatric anaesthesia, especially alerting those units with fewer specialists.

Conclusion

This study showed a prevalence of LS ten times that of HIC, and has reaffirmed the inverse relationship between the income of a country and the likelihood of developing a critical adverse event, namely laryngospasm, indicating the need for resources, education, and quality improvement. The independent risks identified are like those described in the literature, but an important additional information is that the presence of a specialist (consultant) anaesthetist in the operating room during the induction, maintenance, and emergence from anaesthesia is highly protective. The combined technique of using inhalational induction together with a “smidge” of propofol may not be a suitable technique for developing an adequate plane of anaesthesia for airway manipulation. The use of a muscle relaxant, given that safe bag-mask ventilation has been safely established, may help reduce laryngospasm and should be considered. Finally, a careful assessment of the patient peri-operatively in liaison with a specialist anaesthetist may help reduce the prevalence and risk factors associated with laryngospasm, especially in the preschool age group.

Limitations and strengths

Data collection for the study relied on multiple people to collect and complete the CRF. In conjunction with the diagnosis of LS being left to the discretion of the attending anaesthetist, over- or under-reporting was possible, skewing the true prevalence of LS in the study population. Treatment options for LS included the use of propofol and suxamethonium, but these agents were also used at co-induction or during an RSI (Rapid Sequence Induction), thus confounding the finding that suxamethonium and the use of co-induction were independently associated with the occurrence of LS. However, the number of patients treated with suxamethonium and propofol for LS was small compared to their overall use. The association of LS with co-induction and suxamethonium can be explored in future studies to confirm these associations as independent risks. Strengths: This study was a large, multi-centre, prospective observational study. Forms were completed timeously and soon after the incident occurred, with no retrospective gathering of data.

Recommendations

Anaesthetists should be aware of the independent risks associated with laryngospasm as identified in this study and ensure such children are managed by a specialist anaesthesiologist or referred to a centre with a specialist



anaesthesiology presence. Specific risks that can be readily pre-identified include preschool children, those with a current or recent URTI, and those for whom airway surgery (shared airway) or urological surgery is planned.

Alterations to anaesthesia technique which may be beneficial include ensuring adequate depth of anaesthesia before attempted airway device placement, and anticipation of LS during placement of an SGAD, or if neuromuscular blockers are not going to be used, as these are independent risks for LS. Inhalational anaesthesia, although very popular, also increases the risk of LS, as does the use of a co-induction technique (inhalation plus another medication). Anaesthesiologists should therefore consider the use of an intravenous induction in children at higher risk for LS.

Finally, as most LS events occurred at emergence from anaesthesia, enhanced vigilance should be maintained throughout the anaesthetic and not just at induction.

Conflict of interest

The authors declare no conflict of interest.

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List of abbreviations

aOR	Adjusted Odds Ratio
ASA	American Society of Anaesthesiologists
BMV	Bag mask ventilation
CHD	Congenital heart disease
CI	Confidence interval
CPAP	Continuous positive airway pressure
CRF	Case record form
DA	Diploma in Anaesthesia
ENT	Ear, nose, and throat
ETT	Endotracheal tube
GORD	Gastroesophageal reflux disease
HIC	: High-income country
ICU	Intensive care unit
LIC	Low-income country

LMIC	: Low-middle income country
LS	Laryngospasm
MIC	Middle-income country
NMB	Neuromuscular blocker
OR	Odds Ratio
PRAE	Peri-operative respiratory adverse events
RSI	Rapid sequence induction
SD	Standard deviation
SGAD	Supraglottic airway device
TIVA	Total intravenous anaesthesia
URTI	Upper Respiratory Tract Infection

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Data availability

Anonymised data supporting this research can be provided by the authors on request.

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