ARTICLE

Endoscopic evaluation of neonates with signs of upper airway obstruction in the neonatal unit of a tertiary hospital

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INTRODUCTION: The aim of the study is to evaluate major causes of upper airway obstruction in newborns receiving healthcare at our institution, their method of endoscopic assessment and the rate of complications related to these procedures. Materials and methods: This is a case series study of patients from institutional neonatal intensive care unit (NICU) presenting signs of ventilatory dysfunction for whom an endoscopic airway assessment was warranted. Information of interest was collected from medical records according to a Clinical and Endoscopic Assessment Protocol created for the study. The protocol included clinical manifestations needing ENT evaluation, clinical signs of ventilatory dysfunction, comorbidities (pulmonary, cardiac, neurological, and gastrointestinal), examination method (airway endoscopy under general anesthesia or awake), exam complications, and final diagnosis. Results: One hundred sixty-nine newborn patients who underwent airway endoscopy (awake bedside flexible fiberoptic laryngoscopy (FFL) or direct laryngoscopy and bronchoscopy (DLB) in the surgical ward) were included. Thirty-nine patients (23.07%) underwent bedside FFL. For the remaining 130 who underwent DLB under general anesthesia, the median procedure time was 30 min (20–44). Only 9 (5.32%) patients presented complications: desaturation (4), laryngospasm without desaturation with spontaneous resolution (2), apnea with resolution after stimulation (1), seizures (1), nasal bleeding (1). The most frequent diagnoses found were glossoptosis, posterior laryngeal edema, and laryngomalacia.
CONCLUSION: This retrospective case series describes the prevalence of different pathologies that cause upper airway obstruction in neonates. Airway endoscopy seems an effective and safe diagnostic tool in neonatal airway obstruction. Glossoptosis was the most prevalent cause of obstruction in our center.

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INTRODUCTION

Airway disorders have been a common cause of admission to neonatal intensive care units (NICU) [1]. The identification of upper ventilatory distress and/or craniofacial malformations by neonatologists suggest that a possible obstructive airway pathology leads to the need for a specialized assessment to define a correct diagnosis and subsequent management [2].

Endoscopic airway evaluation, which consists of flexible laryngoscopy, direct rigid laryngoscopy, and/or flexible bronchoscopy, is an important ally carried out by ENT in the investigation of patients with signs suggestive of upper airway obstructive diseases. In a neonate who presents with stridor, retractions, cyanosis, and/or desaturations (and sometimes with concomitant dysphagia), any of these examinations may be performed, depending on the suspected pathology. Endoscopic airway evaluation is considered a minimally invasive and low-risk procedure. Nonetheless, description of complications of the exam in the neonatal population is still scarce in the literature.

Among the causes of obstruction, laryngomalacia has been classically described as the most common cause of stridor in term neonates, almost always presenting after the second week of life. However, the increase in survival rate for preterm babies and the fact that this population more frequently needs an NICU admission have resulted in a growing incidence of diagnoses of other congenital airway pathologies before hospital discharge (for example, glossoptosis due to Robin Sequence and congenital subglottic stenosis).

Knowledge of the profile of diseases causing airway obstruction in children admitted to NICU facilitates their early recognition, effective investigation, and treatment. Their frequency, however, varies widely among populations studied, depending on regional characteristics and resources. Currently, most reports still rely on older studies [4, 5] and book chapters [6–8]. There are just a few investigations on the prevalence of airway diseases in neonates and unfortunately the latest reports were published in the beginning of the 21st century [9, 10], or in older babies [11].

Considering the status of our institution as regional reference in pediatric craniofacial and airway diseases, and the growing number of otorhinolaryngological consultation in recent years due to ventilatory dysfunction, upper airway obstruction in the neonate population has become a crucial topic of investigation for our staff. Additionally, choice of diagnostic method and risks of

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these examinations remain a topic for discussion. Bearing this in mind, we have retrospectively evaluated information on all patients eventually undergoing endoscopic examination by our team during a whole decade of NICU consultation.

METHODS

In order to identify the population to be reviewed, a list of all NICU ENT evaluations in the last 10 years (2010–2019) at the study site was requested. From retrieved patients, only those with suspected upper airway obstruction, in which airway endoscopy was performed, were included. Loud breath sounds (stridor or snoring), cyanosis, apnea, desaturation, and retractions were the clinical signs considered as indicators of obstructive ventilatory dysfunction in newborns.

Usually, endoscopic airway evaluation was initially performed by bedside awake flexible laryngoscopy (Pentax fiber-optic-laryngoscope, with an outer diameter of 2.7 mm). Patients were positioned across the bed, without neck hyperextension, while oximetry and cardiac monitoring were maintained. The patient was immobilized by the nursing staff, and a lidocaine hydrochloride 2% gel was applied in the nasal cavity and around the endoscope. After this examination, if the diagnosis was not clear or if there was a suspicion of a disease that could only be diagnosed under general anesthesia (e.g., glossoptosis, congenital subglottic stenosis, subglottic hemangioma), a flexible bronchoscopy, and a rigid bronchoscopy under general anesthesia were performed. General anesthesia was also the choice for intubated babies with a history of difficult intubation.

The patients' medical records were reviewed in order to complete the clinical data assessment protocol designed by the researchers. Clinical, epidemiological, and anthropometric data (gender, age, gestational age, weight, length, clinical manifestations, Apgar score, delivery method) were collected, as well as feeding route and ventilation status at the time of evaluation. In addition to these variables, the maternal gestational complications and patient comorbidities were listed when present. Regarding the latter, they were divided into groups according to the affected system: pulmonary diseases (bronchopulmonary dysplasia, pneumothorax, pulmonary atresia, pulmonary arterial hypertension, bronchopneumonia, respiratory distress syndrome), cardiac (atrial septal defect, ventricular septal defect, patent ductus arteriosus, biventricular hypertrophy, hypertrophic cardiomyopathy, situs inversus, complex cardiac malformation, shunts), gastrointestinal (gastroschisis, duodenal atresia, enterocolitis, gastroesophageal reflux disease, esophageal atresia), neurological (seizures, central nervous system tumor), craniofacial malformations (microcephaly, cleft palate, facial dysmorphia, short lingual frenulum, macrosomia, bilateral congenital glaucoma), and other abnormalities (jaundice, hypothyroidism, renal disorders, congenital syphilis, alcoholic embryopathy and spinal malformations).

All the endoscopy airway descriptions were reviewed. The diagnoses found and the complications of the exams, such as desaturation and laryngospasm, were listed.

Data were collected in an electronic spreadsheet and analyzed using SPSS software version 23.0. Continuous variables were described as mean and standard deviation and median and interquartile range according to their distribution assessed using the Shapiro-Wilk test. Categorical variables were described using absolute and relative frequency.

RESULTS

A total of 254 ENT evaluation requests were identified during a 10-year period. Nine (3.54%) of them comprised otological reasons. Seventy-six (29.92%) were excluded because assessment did not warrant an airway endoscopy, due to clinical improvement or a finding compatible with a disorder not needing an endoscopic evaluation. A total of 169 neonates underwent airway endoscopy at bedside or at surgical ward due to suspected airway obstruction, and were included. Patient characteristics are described in Table 1.

Fifty-one patients (30.2%) had no comorbidity. Among the others, 48 patients had 1 comorbidity; 40, 2 comorbidities; 24, 3 comorbidities; 4, 4 comorbidities, and 2 patients had 5 comorbidities.

Desaturation was the most frequent clinical disturbance (104 patients; 61.5%), followed by stridor (88 patients; 52.1%), and retractions (74 patients; 43.8%).

Table 1. Patients' characteristics.

	***n* (%) or median (p25–75)**
Male	98 (58%)
Gestational age (weeks)	37 (33–39)
Age at consultancy (days)	5 (2–20.5)
Weight at birth (grams)	2845 (1815–3332)
Vaginal delivery	81 (47.9%)
Apgar 1	8 (5–8)
Apgar 5	9 (8–9)
Age at the airway evaluation (days)	8 (3–25.7)
Clinical signs	
Desaturation	104 (61.5%)
Stridor	88 (52.1%)
Retractions	74 (43.8%)
Cyanosis	72 (42.6%)
Dysphagia	72 (42.6%)
Apnea	46 (27.2%)
Micrognathia	43 (25.4%)
Failure to thrive	8 (4.7%)
Ventilatory support	
Oxygen by catheter	31 (18.3%)
Non-invasive ventilation	23 (13.6%)
Invasive ventilation	17 (10%)
Feeding	
Nasogastric tube	90 (53.3%)
Comorbidities	
Cardiac	34 (20%)
Pulmonary	32 (18.8%)
Neurologic	30 (17.6%)
Congenital malformation	23 (13.5%)
Syndrome	18 (10.6%)
Gastrointestinal	17 (10%)
Total length of hospital stay (days)	7 (2–22)

The diagnoses of airway obstruction were listed according to the results of the airway endoscopy (Table 2). More than one third of patients evaluated (34.9%) presented no abnormal findings on airway endoscopy. The most prevalent finding was glossoptosis, present in 49 neonates (28.9%). Isolated posterior laryngeal edema was found in 26 patients (15.4%).

Table 3 shows which diagnoses were found on patients with specific physical findings (desaturation, cyanosis, stridor, retractions).

Micrognathia, observed by the neonatologist, was the reason for evaluation in 43 patients (25.4%). Among these, 29 (67.4%) presented glossoptosis at the endoscopic evaluation. Other diagnosEs found in these babies included laryngomalacia and pharyngomalacia, and some of them presented normal airways (Table 4).

Thirty-nine patients (23%) underwent only bedside FFL (awake endoscopy). Of the 130 who underwent airway endoscopy evaluation under general anesthesia, the median procedure time was 30 min (20–44). Nine (5.3%) patients presented complications during the examination: desaturation [4], laryngospasm without desaturation, with spontaneous resolution [2], apnea with resolution after stimulation [1], seizures [1], and nasal bleeding [1]. The neonate who presented seizures (stiffness, opistothonus, and salivation) at the end of the examination had no previous history of neurological disorder, but presented apnea at birth requiring

orotracheal intubation for a few hours, remaining extubated until evaluation.

From those 130 patients who underwent airway endoscopy under general anesthesia, 17 were intubated at the moment of the examination: 12 presented extubation failure, 3 presented choanal atresia (these patients underwent complete airway examinations and surgery at the same time), and 2 had a history of difficult intubation.

Five patients were on CPAP (continuous positive airway pressure), and two of them progressed to endoscopically-aided tracheal intubation. Two were tracheostomized, one at the delivery room and the other due to multiple failed extubation attempts.

Table 2. Diagnoses.

Diagnosis	*N* (%)
Normal airway	59 (34.9)
Glossoptosis	49 (28.9)
Laryngeal posterior edema	26 (15.4)
Laryngomalacia	21 (12.4)
Vocal fold paralysis	14 (8.3)
Pharyngomalacia	11 (6.5)
Post-intubation acute laryngeal injury	7 (4.1)
Choanal atresia	5 (3)
Nasal stenosis (Pyriform aperture stenosis or Maxilar hypoplasia)	2 (1.2)
Tongue base cyst	2 (1.2)
Tracheomalacia	2 (1.2)
Acquired subglottic stenosis	1 (0.6)
Congenital tracheal stenosis	1 (0.6)
Nasal septal deviation	1 (0.6)
Nasal synechiae	1 (0.6)

Table 3. Diagnoses found in children with specific clinical signs.

Stridor ($n = 88$)	Glossoptosis = 27 (30%)
	Normal airway = 20 (22.7%)
	Laryngomalacia = 15 (17%)
	Laryngeal posterior edema = 14 (15.9%)
	Vocal fold paralysis = 11 (12.5%)
	Pharyngomalacia = 9 (10.2%)
	Other diagnoses = 12 (13.6%)
Cyanosis ($n = 72$)	Glossoptosis = 25 (34.7%)
	Normal airway = 24 (33.3%)
	Laryngeal posterior edema = 11 (15.2%)
	Laryngomalacia = 4 (5.5%)
	Other diagnoses = 11 (15.3%)
Desaturation ($n = 104$)	Normal airway = 34 (32.7%)
	Glossoptosis = 33 (31.7%)
	Laryngeal posterior edema = 19 (18.3%)
	Laryngomalacia = 11 (10.6%)
	Vocal fold paralysis = 6 (5.8%)
	Other diagnoses = 17 (16.3%)
Retractions ($n = 74$)	Normal airway = 19 (25.7%)
	Glossoptosis = 19 (25.7%)
	Laryngomalacia = 13 (17.6%)
	Laryngeal posterior edema = 10 (13.5%)
	Pharyngomalacia = 8 (10.8%)
	Vocal fold paralysys = 8 (10.8%)
	Choanal atresia = 5 (6.7%)
	Other diagnoses = 8 (10.8%)

DISCUSSION

Unlike other traditional reports from the 90s, and also more contemporaneous case series such as Moreddu et al. [12], where laryngomalacia is identified as the main cause of respiratory dysfunction, the present study found glossoptosis as the most frequent etiology for this disturbance in neonates. Glossoptosis is characterized by the posterior collapse of the base of the tongue, which can cause different degrees of respiratory obstruction. The diagnosis is suggested by micrognathia and obstructive symptoms—it is called Robin Sequence when all these features are presented. This condition may be an isolated disorder, or may even be associated with other craniofacial malformations (syndromic or not) [13]. Not all the patients with micrognathia will present glossoptosis at further evaluation, which highlights the value of airway endoscopy. In this study, we found that only 29 out of the 43 babies with micrognathia eventually presented glossoptosis at the endoscopic evaluation. Other diagnosis may also be presented in these babies with micrognathia.

One of the possible reasons for this difference comparing this study with other studies in the literature is that our population comprises younger neonates (average 8 days). This is probably due to the characteristic of our population and also due to the prompt identification of the airway obstruction in neonates by the assistant team and the availability of the ENT staff to assist neonatal patients as soon as consultation is requested. This may also have contributed for an augmented frequency of Robin sequence, since patients already show signs of airway obstruction from birth, requiring earlier evaluation. Moreddu et al. and Lubianca et al. in their studies on the prevalence of diseases that cause stridor in childhood, described populations of older children, with a mean of 2 months and 19 months, respectively. In the study by Saravanam et al. [3], the children's mean age was 56 months. According to other studies, a slight male predominance was found, without a clear explanation [4, 9, 12].

Laryngomalacia was the third most prevalent diagnosis found (12.4%), even less common than isolated posterior laryngeal edema (15.4%) which, although not a disease itself, may be associated with gastroesophageal reflux. Moreddu et al. [12] presents in their case series this same finding in 21.1% of patients, describing posterior laryngeal edema as an important cause of stridor and respiratory dysfunction in newborns, with a good response to proton pump inhibitors (although not randomized to placebo). The lower prevalence of laryngomalacia in the study may reflect a population of infants with a few days of life and moderate to severe upper respiratory obstruction.

Table 4. Diagnoses found in children with micrognathia.

Micrognathia ($n = 43$)	Glossoptosis = 29 (67.4%
	Normal airway = 10 (23.2%)
	Pharyngomalacia = 4 (9.3%)
	Laryngomalacia = 4 (9.3%)
	Vocal fold paralysis = 2 (4.6%)
	Laryngeal posterior edema = 2 (4.6%)
	Choanal atresia = 1 (2.3%)

Berkowitz et al. published a prospective study with 110 neonates with a population younger than 6 months, similar to the population in our study, showing the accuracy of airway endoscopy with the patient awake and the absence of complications. In this study, vocal fold paralysis was the most frequent cause of airway obstruction, followed by laryngomalacia and glossoptosis [14]. In our series, vocal fold paralysis appears as the fourth most commonly found alteration.

Acute intubation lesions were present in only 7 of the 169 neonates who underwent airway endoscopy. Unlike older patients, neonates have a greater tolerance to the presence of a tracheal tube, often remaining on ventilatory support with little or even no sedation and developing fewer traumatic lesions in the larynx and trachea. This data also confirms the improvement in respiratory care by the NICU team.

A significant proportion of patients presented no alterations during airway endoscopy, showing the difficulty to interpret the signs of respiratory dysfunction in newborn patients, who may present comorbidities and other complex cardiac, neurological or low-airway diseases that present with similar clinical signs. In these cases, patient clinical follow-up and subsequent examinations may reveal the cause of the signs presented. In addition, due to the immediate availability of the ENT team to assist these patients and perform airway examination, often mild and/or intermittent obstructive conditions are promptly identified and no significant airway lesion is found. Generally, the patient improves and shows no more signs of obstruction.

Airway endoscopy is a fast and, when well indicated, safe examination, considered the gold standard in the evaluation of the newborn's airway [5, 14, 15]. It can be performed with the patient awake or under general anesthesia, the latter in cases where the airway is not properly visualized, in cases of subglottic or tracheal diseases or abnormalities in the lower respiratory tract are suspected. Signs of upper airway obstruction, such as stridor, retractions and desaturations in the absence of a pulmonary or cardiac cause should always prompt an endoscopic evaluation to make a diagnosis. We should never leave a baby with signs of upper airway obstruction without an endoscopic diagnosis, because of the risks of sudden complete obstruction (as in lingual cysts and subglottic stenosis) and because of the potential long-term complications (as in patients with glossoptosis with apneas and feeding difficulties).

Regarding complications of airway endoscopy in babies, Veras reported transient hypoxemia ($SatO_2 < 94\%$) during procedures in four patients (13.7%) out of 29 neonates less than 30 days old who underwent flexible bronchoscopy, that were not associated with bradycardia and promptly reversed with increased oxygen supply [10]. De Blic et al. described a low rate of complications in 1328 exams performed with awake patients. Minor complications (4.14%) included transient desaturation episodes, excessive cough, nauseous reflex, and epistaxis, and major complications were much less frequent (1.7%) including desaturation below 90%, both alone and associated with laryngospasm, cough, bronchospasm, and pneumothorax. According to Midulla, after the procedure, neonates remain at risk of complications and require close monitoring. Apnea, hypoxia and bradycardia are common and therefore had to be monitored and treated [1]. In the present study, we had no complications in the exams performed with the patients awake and only complications considered minor if performed under anesthesia.

In a study of Hartzell, 241 children were evaluated by airway endoscopy, and 31 of them were submitted to sedation according to criteria established by the author. There were no complications reported. Generally, the indication of examination under general anesthesia depends on the clinical suspicion and the impossibility of the airway endoscopy in awake patient to confirm the presumptive diagnosis [16].

A proposed management flowchart is presented in Fig. 1, aiming to contribute to an optimized care and accurate choice of potential treatments.

CONCLUSION

This retrospective case series contributes to the knowledge on the prevalence of disorders that may cause upper airway obstruction in neonates, since there are no updated prevalence studies in this particular population. Airway endoscopy, both awake and under general anesthesia, seems a safe diagnostic tool in the assessment of neonatal airway obstruction. Glossoptosis was the most prevalent cause of obstruction in our center and the different findings in the literature can be explained by peculiarities in patient referrals. Considering that the tertiary centers of care for newborns have their own particularities, it is important to know

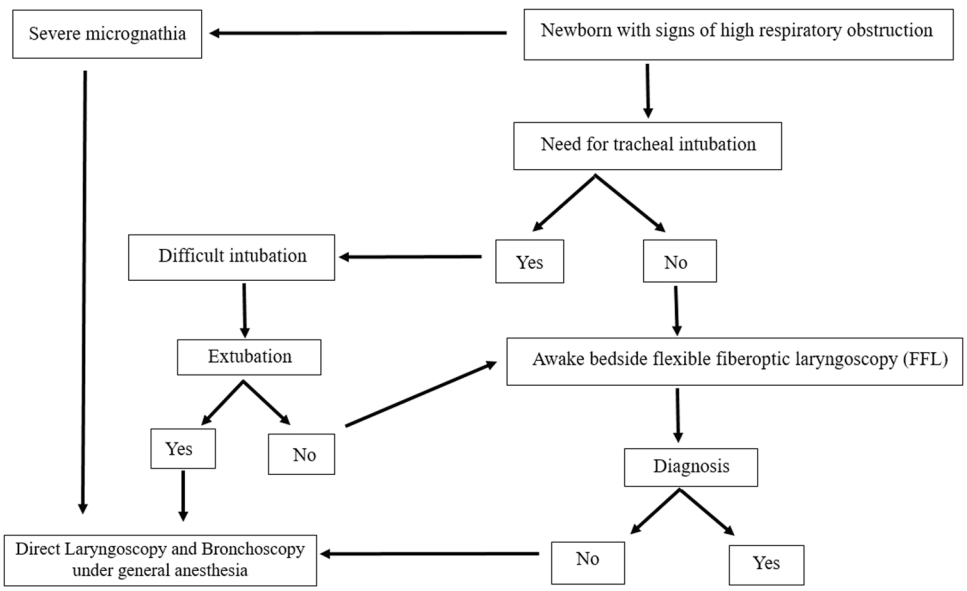

Fig. 1 Upper respiratory obstruction investigation flowchart in neonates. Steps of investigation of neonates with signs of respiratory obstruction.

the population and conduct the investigation based on epidemiological data and clinical history and examination.

DATA AVAILABILITY

The datasets generated during and/or analyzed during the current study are available in http://www.ufrgs.br. All data generated or analyzed during this study are included in this published article.

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AUTHOR CONTRIBUTIONS

LPK: wrote final drafts of the manuscript. LK: data collect. DM: analysis of data for the work RSP: Highlights somepoints in the investigation and detailing of the study. PJCM: conception or design of the work. CS: approved the final published version, and are accountable for all aspects of the manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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