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Etiological profile of upper airway obstruction in infants

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Abstract

Background: Respiratory distress is recognized as any sign of breathing difficulty in infants. Some congenital anomalies present immediately with airway distress, while others are asymptomatic or discovered later in infancy or childhood. Our objectives are to detect different laryngeal causes of respiratory distress in infants and to measure the relative risk of some variables like age, sex, family history, and other congenital anomalies for developing laryngeal causes of respiratory distress. This observational cross-sectional study was carried out during the period from June 2017 to December 2018 at Children's University Hospital. The study included 80 infants who presented with respiratory distress and admitted to the hospital. All patients subjected to a detailed history from their parents and full general and ENT examinations. X-ray, MSCT neck or direct laryngoscope were carried out in selected cases.

Results: As regard age, 58% of cases were between 1–6 months, 28% of cases between 6 months and 1 year, and 14% between 1–2 years. Laryngeal causes of respiratory distress among infants were distributed as follow: 70% laryngomalacia, 18% subglottic stenosis, 8% laryngeal web, and 4% of cases were caused by vocal fold paralysis (VFP). The laryngeal causes of respiratory distress did not reveal any statistically significant difference among different age groups or between both genders ($P = 0.257$, 0.286; respectively). Also, there was no statistically significant difference between infants with positive family history and those without as regard the laryngeal causes of respiratory distress ($P = .378$).

Conclusion: The majority of respiratory distress cases (58%) were between 1–6 months. Bivariant analysis of variables age, sex, family history, and other congenital anomalies showed that they were not potent risk factors for developing laryngomalacia, subglottic stenosis, laryngeal web, and vocal fold paralysis. Laryngomalacia represented the commonest cause of respiratory distress (70%) followed by subglottic stenosis (18%), then laryngeal web (8%), and finally the vocal fold paralysis represented the least percentage (4%). Apart from laryngomalacia, the percentages of other causes seem to vary according to sample size and geographic area of study. So, being familiar with the common causes of respiratory distress in a given region is very essential in order not to miss a potentially life-threatening diagnosis.

Keywords: Infants, Laryngeal, Respiratory distress, Laryngomalacia

Background

Respiratory distress is recognized as any sign of breathing difficulty in infants. It is a common problem in the early neonatal and infant period occurring in up to 7% of infants [1]. Stabilization of the infant and early recognition of the etiology helps in minimizing complications and ensuring appropriate definitive therapy [2]. Stridor is a loud, harsh, and high-pitched respiratory sound. It is usually heard on inspiration due to partial obstruction of the airway (usually extra-thoracic—that is, in the trachea, larynx, or pharynx). Stridor can occur on expiration in severe upper airway obstruction but usually indicates tracheal or bronchial obstruction (intra-thoracic). Biphasic stridor suggests subglottic or tracheal

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obstruction [3]. Difficulties at the level of the larynx are commonly associated with stridor or noisy breathing. Some congenital anomalies present immediately with airway distress while others are asymptomatic or discovered later in infancy or childhood as feeding and growing difficulties [4]. Supraglottic anomalies including laryngomalacia, bifid epiglottis, saccular cyst, and laryngeal cleft affect the airway at the level of the epiglottis through the ventricle, which sits immediately superior to the vocal folds [5]. Laryngomalacia is the most common cause of stridor in newborns, affecting 45–75% of all infants with congenital stridor. Most infants with laryngomalacia will have mild symptoms and a benign disease course that resolves by the age of 12 to 24 months; however, it is important to recognize that not all cases of laryngomalacia have a benign course [6]. Glottic anomalies affect the airway involving the vocal folds and lead to a dysphonic or aphonic cry and may also present with stridor. It includes vocal fold paralysis (VFP) and laryngeal/glottic web [7]. In the current research, we studied different causes of respiratory distress in a certain period of time to show the distribution of different causes of upper airway obstruction in infants and any possible risk factors. This is important to make otolaryngologists and pediatricians familiarize with every diagnosis and its possibility in our population in order to properly manage these potentially fatal conditions. Our objective in the current research is to reveal the etiological profile of respiratory distress in infants including possible relative risk of certain variables.

Methods

In this observational cross-sectional study, all methods and procedures were conducted in the period from June 2017 to December 2018 according to the Institutional Review Board of the Faculty of Medicine. Also, the study was approved by the Institutional Ethical Committee of the Faculty. Written informed consents were obtained from all parents. All patients were recruited from Children's University Hospital. This study included 80 infants (32 females and 48 males) with age range from 1 month to 2 years who presented in the study period. All included infants presented with respiratory distress. Patients with bronchial asthma or other chest diseases were excluded from the study. Detailed history taking was carried out including age, gender, family history of laryngeal congenital anomalies, and symptoms of respiratory distress (e.g., difficult breathing, grunting, and stridor). Careful general examination was done searching for any nasal flaring, cyanosis, respiratory rate, suprasternal, intercostal, and subcostal in-drawing. Also, full laryngeal examination was performed including laryngeal endoscopy by fiberoptic nasopharyngolaryngoscopy with HD headcam, Karl Stors tele pack X LED. In addition,

DL and radiological investigation (X-ray, multi-slice computer tomography (MSCT) for the neck) were carried out in selected cases. Moreover, every patient underwent complete blood count, serum calcium level, and random blood sugar. In this study, Monte Carlo exact p test used as it is a statistical package for analyzing continuous or categorical data. The goal in the exact test is to enable researcher to make reliable interference when data are small, when requirement of each cell in data entry is less than 5 cases, so relying on the accuracy of exact p value will be put in consideration during dealing with data of this study. Data were present blindly for the statistician to measure any association (relative risk) of some variables (age, sex, and family history) with laryngeal causes of respiratory distress.

Results

This study included 80 infants (32 females and 48 males) with age range from 1 month to 2 years. All cases were stable at the time of first diagnosis in the hospital with no definite cyanosis; however, they revealed some variable degrees of respiratory distress in the form of stridor and suprasternal in-drawing. All laboratory testing was normal. Following fiberoptic laryngoscopy, radiography confirmed diagnosis of subglottic stenosis (14 subjects) and laryngeal web (6 subjects) and excluded any anatomical abnormalities in the trachea. In subglottic stenosis, a narrowing of the subglottic airway in the region of cricoid cartilage was detected by a fiberoptic laryngoscope which is more sensitive than CT by showing small stenosis. Similarly, in laryngeal web, a membrane was seen to extend between the two vocal folds and partially occluded the glottis. These membranes have different thickness and vertical locations. It may be thin or thick and glottic, supraglottic, or subglottic. For the diagnosis of laryngomalacia, the endoscopic findings are retroverted, curled or omega-shaped epiglottis, and soft laryngeal structure with sucked-in aryepiglottic folds during inspiration resulting in laryngeal inlet closure. The vocal fold paralysis represents a challenging diagnosis in our infants because of continuous crying. However, the examiner must concentrate at the end of the cry when the infant takes inspiration to detect if one vocal fold abducts and the other is fixed. Sometimes, the entire vocal fold could not be seen, in this case fixed arytenoid on the affected is enough for the diagnosis especially when the infant has a weak hoarse cry. Bilateral vocal fold paralysis not included in our study. Figure 1 shows an example picture for each diagnosis. Figure 2 illustrates the distribution of different laryngeal causes of respiratory distress in infants. There was no statistical significance difference in age groups between laryngeal causes of respiratory distress (MCP = 0.257) according to the Mont Carlo exact test (Table 1). For laryngomalacia, there are
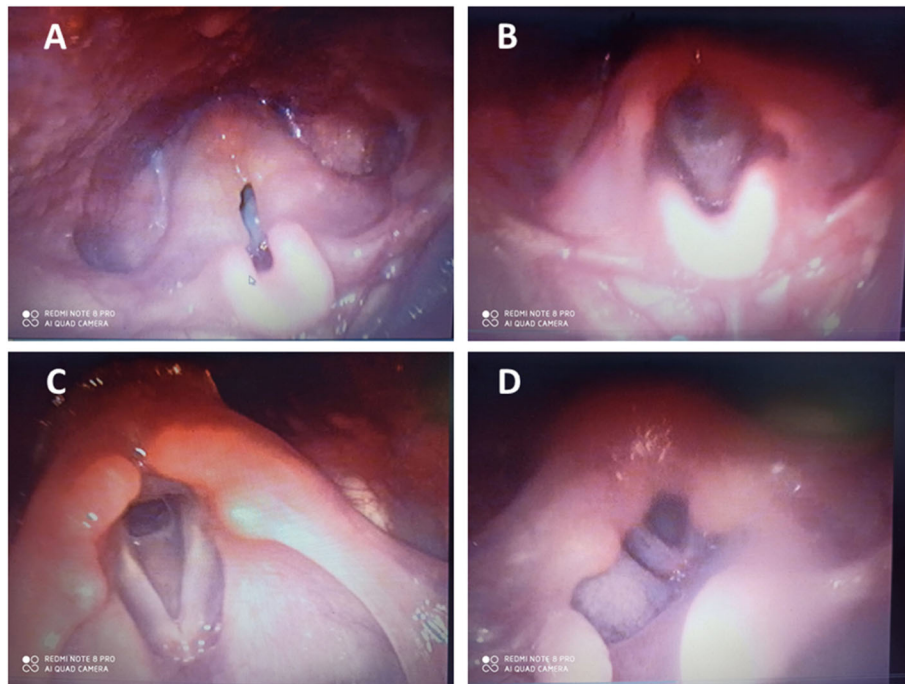
Fig. 1 Causes of respiratory distress. **a** is showing laryngomalacia with curled epiglottis and sucked-in aryepiglottic folds. **b** is showing subglottic stenosis with airway narrowing at the cricoid region. Note that some whitish secretion appears above the stenosis which may be mistaken for laryngeal web. **c** is showing the thin subglottic laryngeal web extending from the undersurface of both vocal folds. Lastly, **d** is showing left vocal fold paralysis with limited vocal fold mobility in abduction

36 cases in the infant age group 1–6 months, 16 cases in the infant age group 6 months to 1 year, and 4 cases from the age group 1 year–2 years. For subglottic stenosis, there are 7 cases from the age group 1 year to 2 years followed by 5 cases in infants aged 6 months to 1 year then only 2 cases in infants aged 1–6 months. All cases (6 cases) who suffered from laryngeal web were recorded in infants aged 1–6 months, while 2 cases of vocal fold paralysis were recorded from the age group 1–6 months and 2 cases from the age group 6 months to 1 year. Moreover, there was no statistically significant difference in the male and female groups between
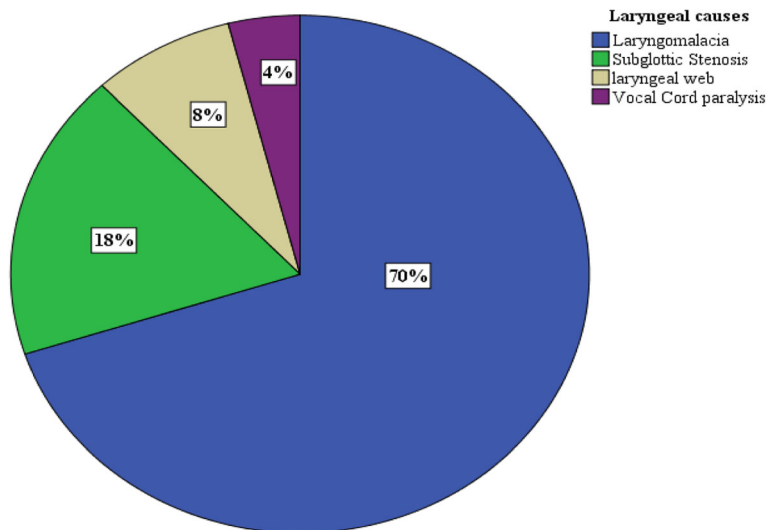

Fig. 2 Laryngeal causes of respiratory distress. This figure represents a pie chart for prevalence of different etiologies of the upper airway obstruction in infants. The laryngomalacia is the commonest cause (70%) followed by subglottic stenosis (18%)

Table 1 Age distribution in different laryngeal causes of respiratory distress in infants

Laryngeal causes	1–6 months (n = 46)		6 months to 1 year (n = 23)		1 year to 2 years (n = 11)		P value
	No.	A.1.1.1.1.1.5. %	A.1.1.1.1.1.4. No.	A.1.1.1.1.1.3. %	A.1.1.1.1.1.2. No.	A.1.1.1.1.1.1. %	
Laryngomalacia	36	78.4	16	69.5	4	36.4	(MCP = 0.257)
Subglottic stenosis	2	4.3	5	21.7	7	63.6	
Laryngeal web	6	13	0	0	0	0	
Vocal fold paralysis	2	4.3	2	8.8	0	0	

MCP Monte Carlo exact *p* value with confidence interval 95%

laryngeal causes of respiratory distress. The majority of cases with laryngomalacia were male, 32 cases vs only 24 females. The same in subglottic stenosis cases, 10 males vs 4 females. There were 3 male cases versus 1 female who have vocal fold paralysis. Males and females were equal in cases of laryngeal web—3 cases for each (Table 2). In addition, there was no statistically significant difference in infants who had a positive family history vs those who had a negative family history (MCP = 0.378). Only 8 cases with family history of the same conditions were detected, 6 cases had family history of laryngomalacia, and 2 cases had one family history of subglottic stenosis (Table 3). Other congenital anomalies were detected in 8 cases; five cases in laryngomalacia, 3 cases in subglottic stenosis and one case in patient with vocal fold paralysis as illustrated in Table 4.

Discussion

Respiratory disorders are the commonest causes of morbidity and mortality in the neonatal period [8]. It is an initial manifestation of a large number of respiratory or non-respiratory disorders like those of central nervous system origin, trauma, cardiac failure, or metabolic disorders. On autopsy, the incidence of respiratory disorders has been found to range from 32 to 54% [9]. In our study, the majority of cases (58%) was between 1–6 months, followed by (28%) cases between 6 months and 1 year, and only 14% between 1 year and 2 years. As regard sex, males constituted 60% of the study sample, while females were 40%. The reason for the difference between the percentages of male and female patients presenting with stridor is unclear. This is in line with

Bjornson and Johnson, & Denny et al., studies who reported that boys were affected more than girls (1.4:1) and young children between 6 months and 3 years of age more commonly than older children and adolescents [10, 11]. Similarly, among the 81 laryngomalacia patients included in *Olgun et al.*'s study, 48 were male, and 33 were female, and the mean age was 4.9 months [12]. Also, among the total of 395 patients who were diagnosed with laryngomalacia and included in study by *Irace et al.*, 92 (64.8%) were males, with a median (interquartile range) age at the time of study of 7.9 (3.2–20.5) months [13]. *Zoumalan et al.*, published a series of 202 infants under the age of 12 months examined for stridor in a specialized unit, 119 (59%) were boys, and 83 (41%) were girls. All patients were less than 1 year of age. Their ages ranged from 3 days to 11 months; 175 (87%) were 6 months of age or younger [14]. In a similar study by *Holinger*, of 219 patients whose primary presenting symptom was stridor, 150 were male, and 69 were female [15]. In 324 children enrolled in *Boogaard et al.*'s study with laryngomalacia, 193 were males with a median (range) age of 4.4 (0 to 18) years [16]. A screening of 1986 consecutive live births done for the evidence of respiratory distress was included in the study by *Nagendra et al.*. Out of the 48 neonates who developed respiratory distress, 25 were males and 23 were females. The male-to-female ratio was 25:23 = 1.08:1 [17]. A higher incidence in males was observed in the present study as well as in various earlier studies [17–19]. In the current study, the variables age, sex, family history, and

Table 2 Distribution of sex among laryngeal causes of respiratory distress

Laryngeal causes	Male (n = 48)		Female (n = 32)		p value
Laryngomalacia	32	66.6	24	75	(MCP = 0.286)
Subglottic stenosis	10	20	4	12.5	
Laryngeal web	3	6.7	3	9.4	
Vocal fold paralysis	3	6.7	1	3.1	

MCP Monte Carlo exact *p* value

Table 3 Distribution of family history among laryngeal causes of respiratory distress

Laryngeal causes	Family history				P Value
	Positive (n=8)		Negative (n=72)		
	No.	%	No.	%	
Laryngomalacia	6	76	50	69.4	(MCP= 0.378)
Subglottic stenosis	2	24	12	16.6	
Laryngeal web	0	0	6	8.5	
Vocal fold paralysis	0	0	4	5.5	

MCP Monte Carlo exact *p* value

Table 4 Distribution of other congenital anomalies among laryngeal causes of respiratory distress

Laryngeal causes	Other congenital anomalies				p value
	(n = 8)		(n = 72)		
Laryngomalacia	5	62.5	51	71	(MCP = 0.222)
Subglottic stenosis	2	25	12	16.6	
Laryngeal web	0	0	6	8.3	
Vocal fold paralysis	1	12.5	3	4.1	

MCP Monte Carlo exact p value

other congenital anomalies are not potent risk factors for developing laryngeal causes of respiratory distress. Moreover, in this study, we found the highest percentage of causes (70%) were due to laryngomalacia, followed by subglottic stenosis (18%) then laryngeal web (8%), while vocal fold paralysis recorded the least percentage (4%). This is consistent with *Jabbour et al.*'s study which included 404 patients with respiratory distress [20]. According to *Escher et al.* & *Thorne and Garetz*'s study, laryngomalacia is the most frequent cause of stridor in newborns and infants and is the underlying reason in 60 to 75% of cases with stridor [21, 22]. In our study, only 5 cases of the 56 cases of laryngomalacia had other airway anomalies (9%); this is in line with the *Yuen et al.*, *Rifai et al.*, & *Dickson et al.* studies which reported that other airway pathologies can accompany laryngomalacia at rates varying from 7.5 to 64% [23–25]. Laryngomalacia is the most common cause of stridor in newborns, affecting 45–75% of all infants with congenital stridor according to *Richter and Thompson* [6]. Similarly, *Daniel and Cheng* reported that laryngomalacia is the commonest cause of neonatal stridor. Subglottic stenosis (SGS) is nowadays seen as relatively infrequent [26]. *Thompson*, reported that laryngomalacia (LM) is the most common laryngeal anomaly in infants [27]. The etiologies of airway obstruction in our subjects were laryngomalacia, subglottic stenosis, vocal fold paralysis, and laryngeal web. Our findings are consistent with *Toews and Weiner* who reported that laryngomalacia is the most prevalent cause of congenital stridor, accounting for 60% of cases [28]. However, unlike our results, they reported that congenital vocal fold paralysis is the next most common cause [19]. Similarly, *Friedman et al.* reported that laryngomalacia is the most common congenital anomaly of the larynx and is the most frequent cause of stridor in infants. It accounts for 60% of laryngeal problems in infants [29]. Other synchronous laryngotracheal anomalies have been reported by *Berg and McClay*, including subglottic stenosis and vocal fold paralysis [30]. Contrary to our study, *Wolter et al.* concluded that vocal fold paralysis (VFP) accounts for 10% of all congenital laryngeal anomalies and is the second most common cause next to laryngomalacia [31]. According to *Zbar and Smith*'s

results, laryngomalacia and subglottic stenosis most frequently affect infants, VFP is a common finding in both infants and adults [32]. The prevalence of associated airway lesions has been more clearly documented according to *Mancuso et al*; laryngeal dyskinesia, vocal fold paralysis, subglottic stenosis are more frequent in infants [33]. In this study, we found that subglottic stenosis represents the second most common cause of respiratory distress (18%). This is inconsistent with some previous reports. *Nicolai* [34] *and Shatla et al.* [35] recorded that paralysis of the vocal folds is the second most common cause of neonatal stridor. Similar results were reported by *Wiatrak*, who founded that the second most common congenital anomaly of the larynx is vocal cord paralysis, accounting for 20% of laryngeal lesions [36]. This disagreement may be due to the limited number of subjects in our study. Also, the relatively difficult diagnosis of subglottic stenosis compared to more obviously seen diagnosis in the larynx could explain possible previous missing diagnosis. Among one hundred two cases of vocal fold paralysis (VFP), studied by *Daya et al.*, most patients (68% (n = 69)) were diagnosed before age 12 months; of these, 65% (n = 45) presented with symptoms at birth [37]. In line with our study, *Daniel*'s study reported that laryngomalacia is the most common congenital anomaly of the larynx. It represents 60% of all congenital laryngeal anomalies. Males are affected twice as often as females [38]. Laryngomalacia incidence was reported to be 1.6 times higher in boys than in girls according to *Landry and Thompson*'s study [39]. *Cukor and Manno* found that laryngomalacia is the most common cause of chronic stridor in children younger than 2 years. It has a male-to-female ratio of approximately 2:1 [40]. Similarly, *Jefferson et al.* found in their study that congenital subglottic stenosis is the third most common congenital anomaly of the larynx. It accounts for 15% of all cases. Males are affected twice as often as females [41]. *Schweiger et al.* reported that the median age of the included children who developed subglottic stenosis was 2.6 months [42]. *Cohen et al.* [43] and *Gentile et al.* [44] also noted a marked male predominance. Among infants with idiopathic VFP (86%). A total of 277 cases with VFP was studied by *Gandhi et al.*, out of which 179 were males, and 98 were females with a male-to-female ratio being 1.82:1 [45]. Similar to the current study, *Bedwell and Zalzal* concluded that most cases of laryngomalacia occur sporadically in people with no family history of the condition [46]. On the other hand, *Chen et al.* reported that laryngomalacia may be inherited in some instances. Only a few cases of familial laryngomalacia (occurring in more than one family member) have been described in the literature [47]. Also, *Gacek* reported a family in which the father and two sons had hereditary bilateral vocal fold paralysis; another, 4 siblings, 1 male

and 3 female, were normal. His patients also had other neurological findings later in life indicating possible association with the laryngeal defect [48].

Limitation
Every study has its own drawbacks. Our study has a limited number of cases; so, further research with a larger sample is recommended before generalization.

Conclusion
The highest percentage of respiratory distress (70%) was due to laryngomalacia, followed by subglottic stenosis (18%) then laryngeal web (8%), while vocal fold paralysis was recorded with least percentage (4%). The importance of determining the cause of stridor cannot be overemphasized, as the majority of infants presenting with stridor have laryngomalacia; however, there are numerous other possible etiologies to consider. Laryngomalacia is a common disease of infancy where the diagnosis is suspected by primary care providers based on history. Subglottic stenosis is the second most common etiology of stridor in our infants. This is important to suspect in order not to miss a relatively difficult and life-threatening diagnosis. Recognizing patient factors and symptoms associated with moderate and severe diseases helps determine which infants will benefit from otolaryngology consultation. Identifying patient factors that influence disease severity and outcomes is an important aspect of counseling caregivers and providing care to infants.

Abbreviations
MSCT: Multi-slice computer tomography; VFP: Vocal fold paralysis

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