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ORIGINAL RESEARCH

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Reflux disease and congenital laryngomalacia in neonates: A Kids' Inpatient Database analysis

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Abstract

Objectives: Congenital laryngomalacia (CLM) is the most common cause of stridor in neonates and is commonly associated with reflux disease (RD) such as gastroesophageal reflux and newborn esophageal reflux. This study investigates the impact of RD on the management and outcomes of neonates with CLM.

Methods: The 2016 Kids' Inpatient Database (KID) was queried for neonates with CLM (ICD-10: Q31.5). RD status, procedures, and complications were identified with ICD-10 codes. Univariate and multivariable analyses were implemented to determine statistical associations.

Results: Of 2212 neonates identified with CLM, 585 (26.45%) had RD. Patients with RD were more often female ($p = .038$) and premature ($p < .001$). Upon multivariable analysis, patients with RD had greater total charges (Mean $457,810.87 vs. $259,020.90, $p < .001$) and longer length of stay (Mean 46.03 vs. 26.44 days, $p < .001$). Those with RD had more diagnoses recorded (Mean 14.15 vs. 9.66, $p < .001$), underwent more procedures (Mean 5.47 vs. 3.49, $p < .001$), and had a longer wait until their first procedure (Mean 13.27 vs. 7.02 days, $p < .001$). Patients with RD had increased odds for undergoing laryngoscopy (OR 1.799, 95% CI 1.382–2.321, $p < .001$), bronchoscopy (OR 2.179, 95% CI 1.598–2.801, $p < .001$), and ventilator use (OR 1.526, 95% CI 1.197–1.886, $p < .001$) on multivariable regression adjusting for patient demographics, hospital characteristics, and comorbidities. Patients with and without RD had similar odds for undergoing tracheotomy (OR 1.540, 95% CI 0.934–2.522, $p = .088$) and mortality (OR 1.084, 95% CI 0.397–2.646, $p = .874$).

Conclusion: CLM is a common diagnosis in neonates that is associated with RD. In our cohort of neonates with CLM, those with RD had overall poorer outcomes.

Level of evidence: 4.

KEYWORDS

congenital laryngomalacia, head and neck surgery, neonate, pediatric, reflux disease

1 | INTRODUCTION

Congenital laryngomalacia (CLM) is the most common laryngeal anomaly in newborns and the most common cause (65%–75%) of stridor in neonates.[1,2] This stridor is typically due to inspiratory phase inward folding and collapse of supraglottic structures.[3,4] Feeding difficulties and inspiratory retractions are among the early presentations, although a flexible laryngoscopy is considered the appropriate diagnostic method for CLM.[5–7] Characteristic findings on flexible laryngoscopy may include omega-shaped epiglottis, short-aryepiglottic folds, and collapsible arytenoid cartilages.[4,8] Although the etiology of CLM remains unknown, the most common explanation includes neuromuscular immaturity.[5,9,10]

Another common hypothesis is that reflux disease (RD) might contribute to CLM progression by potentiating airway obstruction via airway resistance changes and by inducing supraglottic edema.[4,11,12] On the other hand, some posit that CLM can lead to RD by affecting the normal pressure gradient between the thoracic and abdominal cavities, which normally protects against reflux events.[4] Although RD is found in 35%–68% of infants with CLM, it has been suggested that there is not enough evidence to support a causal relationship between RD and CLM.[11,13,14] In addition, antireflux therapy has been documented to provide improved outcomes in certain CLM cohorts, but literature on the clinical effectiveness of antireflux in CLM patients is highly variable and multifactorial.[15,16]

Further supporting the relationship between RD and CLM, some studies have found RD to be associated with increased complications and overall poorer outcomes.[15,17] Although there is extensive literature citing the association between RD and CLM, there is still sparse literature covering the impact of RD on the management and outcomes in patients with CLM. Separately, it has been demonstrated that neonates are associated with poorer outcomes compared to older infants with CLM.[18] Our study aims to utilize a national cohort to provide a characterization of RD in a national cohort of neonates with CLM, as well as to investigate differences in management and outcomes based on RD status.

2 | MATERIALS AND METHODS

The 2016 Kids' Inpatient Database (KID), a part of the Healthcare Cost Utilization Project (HCUP) and sponsored by the Agency for Healthcare Research and Quality (AHRQ), was used in a retrospective review. KID is currently the largest database containing publicly available inpatient pediatric (less than 21 years old) cases within the United States of America.[19] This database provides encounter-level and hospital-level healthcare data from cases in 2016. International Classification of Diseases, 10th Revision (ICD-10), codes were used to create and analyze our cohort. A similar study utilizing 2016 KID to investigate CLM was used as a reference for methodology.[18] Given that the 2016 KID is a federally deidentified database, this study was granted exemption from approval by the Rutgers New Jersey Medical School Institutional Review Board.

We queried KID for the ICD-10 diagnosis code corresponding to CLM (Q31.5). Patients admitted as neonates (age <28 days old) with an ICD-10 code of Q31.5 were included in the cohort. RD status was identified with ICD-10 diagnosis codes for gastroesophageal reflux disease (GERD) (K21, K21.0, and K21.9) and newborn esophageal reflux (NER) disease (P78.83).

Demographic data included sex and race (White, Black, Hispanic, Asian and Pacific Islander, Native American and other). Although patient income data was not directly reported in KID, the national quartile for the median income of the patient's zip code was included. Hospital region within the USA (Northeast, Midwest, South, West) and hospital teaching status (rural, urban/non-teaching, urban/teaching) were included. Although KID does not directly report comorbidities, ICD-10 codes can be used to extrapolate comorbidities within the cohort. To include prematurity in the analysis, the ICD-10 code was utilized (P07.3). Down syndrome (Q90.9), atrial septal defect (Q21.1), and bronchopulmonary dysplasia (P27.1) were also included as comorbidities. Ultimately, demographic and hospital data analyzed by RD status included sex, race, premature status, Down syndrome, atrial septal defect, bronchopulmonary dysplasia, national median income by patient zip code, hospital teaching status, and hospital region.

Total charges, length of stay (LOS), number of diagnoses and procedures documented in the patient chart, time until undergoing their first procedure, and mortality were all reported directly in the database and analyzed by RD status. Additionally, the most commonly performed procedures in this cohort and CLM literature were included in analysis with ICD-10 procedure codes: laryngoscopy (0CJSxx), bronchoscopy (0BJ0xx), tracheotomy (0B11xx), and ventilation (5A19xx). Laryngoscopy included both direct and flexible modalities because of limitations in ICD-10 coding.

Demographics, hospital data, charges, outcomes, and management were analyzed by RD status with univariate analysis. Univariate analysis was primarily performed with the Fischer exact test, but the Pearson chi-square test was used when appropriate. Where appropriate, the mean and standard error of the mean (SE) are reported. Multivariable linear and logistic regressions were performed to compare charges, outcomes, and management, after adjusting for sex, race, income status, hospital region, teaching status, prematurity, Down syndrome, atrial septal defect, and bronchopulmonary dysplasia. Multivariable analysis results are reported as patients with RD compared to the reference (no RD). Marginal values were reported as the adjusted difference in values between RD and reference (no RD) for multivariable linear regression in continuous variables. Odds ratios (OR) were reported for multivariable logistic regression in categorical variables. A p-value of <.05 was considered significant and a 95% confidence interval (CI) was reported as appropriate. All statistical analyses were performed in SPSS version 25 (IBM Corp, Armonk, NY).

3 | RESULTS

2212 patients met the selection criteria for having CLM and being admitted as neonates. Of these patients, 585 (26.45%) had

TABLE 1 Demographic and comorbidity data of neonates with congenital laryngomalacia by reflux disease status.

	Total, $n = 2212$	No reflux disease, $n = 1627$	Reflux disease, $n = 585$	p-value
Sex				
Male	54.1%	55.4%	50.4%	.038
Female	45.9%	44.6%	49.6%	
Race				
White	50.2%	50.2%	50.0%	.882
Black	15.2%	14.7%	16.9%	
Hispanic	22.3%	22.8%	21.1%	
Asian-Pacific Islander	4.3%	4.4%	4.2%	
Native American	1.1%	1.1%	1.1%	
Other	6.8%	6.8%	6.7%	
Prematurity				
Premature	18.8	15.6%	27.5%	<.001
Full term	81.2	84.4%	72.5%	
Down syndrome				
Comorbidity incidence	4.4%	3.7%	6.5%	.007
Atrial septal defect				
Comorbidity incidence	27.6%	22.6%	41.7%	<.001
Bronchopulmonary dysplasia				
Comorbidity incidence	4.4%	4.5%	4.3%	.907
Median Income Quartile – Patient Zip Code				
0–25%	29.5%	28.0%	33.6%	.049
26%–50%	25.4%	25.5%	25.1%	
51%–75%	23.4%	23.7%	22.5%	
76%–100%	21.7%	22.8%	18.8%	
Hospital region				
Northeast	17.5%	18.4%	14.7%	.001
Midwest	24.5%	25.6%	21.5%	
South	34.9%	32.6%	41.4%	
West	23.1%	23.4%	22.4%	
Hospital teaching status				
Rural	2.1%	2.6%	0.5%	<.001
Urban/Non-teaching	11.3%	12.7%	7.2%	
Urban/Teaching	86.7%	84.6%	92.3%	

RD. Specifically, 514 had NER and 74 had GERD, with three patients being diagnosed with both. Neonates with RD were more likely to be female than those without RD (49.6% vs. 44.6%, $p = .038$) (Table 1). Patients with RD were more likely to be premature (27.5% vs. 15.6%, $p < .001$), have Down syndrome (6.5% vs. 3.7%, $p = .007$), an atrial septal defect (41.7% vs. 22.6%, $p < .001$), a lower national income quartile by zip code ($p = .049$), and be treated at an urban teaching hospital (92.3% vs. 84.6%, $p < .001$) compared to those without RD. Although hospital region ($p = .001$) varied between those with and without RD, there were no significant differences in racial distribution ($p = .882$).

Univariate analysis indicated that neonates with RD had greater total charges than those without (Mean $457,810.87 vs. $259,020.90, $p < .001$) (Table 2). When adjusting for demographic, comorbidity, and hospital data on multivariable analysis, it was demonstrated that patients with RD were marginally charged $179,823.44 (95% CI $118,992.19–$250,846.18) more than those without RD (adjusted $p < .001$) (Table 3). Patients with RD had longer LOS than those without (Mean 46.03 vs. 26.44 days, $p < .001$, Marginal 17.981 days, adjusted $p < .001$). Moreover, those with RD had more diagnoses (Mean 14.15 vs. 9.66, $p < .001$, Marginal 3.583, adjusted $p < .001$) and procedures (Mean 5.47 vs. 3.49, $p < .001$, Marginal 1.322, adjusted $p < .001$) recorded. Those with RD also had a longer wait until they underwent their first procedure (Mean 13.27 vs. 7.02 days, $p < .001$, Marginal 4.982 days, adjusted $p < .001$).

TABLE 2 Charges and outcomes of neonates with congenital laryngomalacia by reflux disease status.

	Total	No reflux disease	Reflux disease	Reflux disease status *p*-value
Total charges (Mean $ [SE])	$ 311,919.40 [$13,619.72]	$ 259,020.90 [$15,057.71]	$ 457,810.87 [$29,071.22]	<.001
Length of stay (Mean days [SE])	31.62 [1.03]	26.44 [1.14]	46.03 [2.17]	<.001
Number of diagnoses (Mean [SE])	10.85 [0.16]	9.66 [0.17]	14.15 [0.31]	<.001
Number of procedures (Mean [SE])	4.01 [0.09]	3.49 [0.11]	5.47 [0.20]	<.001
Time until 1st procedure (Mean days [SE])	8.85 [0.51]	7.02 [0.52]	13.27 [1.18]	<.001
Mortality (%)	1.3%	1.3%	1.4%	.514
Laryngoscopy (%)	32.9%	28.6%	44.6%	<.001
Bronchoscopy (%)	16.5%	12.9%	26.7%	<.001
Tracheotomy (%)	3.7%	3.1%	5.3%	.012
Ventilation (%)	21.2%	18.4%	29.1%	<.001

TABLE 3 Adjusted multivariable analysis (with marginal values and odds ratios [ORs]) of charges and outcomes in neonates with congenital laryngomalacia associated with reflux disease.

	Adjusted OR (reference: no reflux disease)	95% CI	*p*-value
Total charges (Marginal $)	179,823.44	(118,992.19–250,846.18)	<.001
Length of stay (Marginal days)	17.981	(12.823–22.475)	<.001
Number of diagnoses (Marginal number)	3.583	(2.038–4.811)	<.001
Number of procedures (Marginal number)	1.322	(1.002–2.103)	<.001
Time until 1st procedure (Marginal days)	4.982	(3.233–7.495)	<.001
Mortality	1.084	(0.397–2.646)	.874
Laryngoscopy	1.799	(1.382–2.321)	<.001
Bronchoscopy	2.179	(1.598–2.801)	<.001
Tracheotomy	1.540	(0.934–2.522)	.088
Ventilation	1.526	(1.197–1.886)	<.001

Note: Multivariable analysis adjusting for sex, race, income status, hospital region, teaching status, prematurity, Down syndrome, atrial septal defect, and bronchopulmonary dysplasia.

Multivariable analysis adjusting for confounding factors including patient demographics, hospital characteristics, and comorbidities demonstrated that mortality was similar between those with and without RD (OR 1.084, 95% CI 0.397–2.646, adjusted $p = .874$). Patients with RD had increased odds for undergoing laryngoscopy (OR 1.799, 95% CI 1.382–2.321, adjusted $p < .001$), bronchoscopy (OR 2.179, 95% CI 1.598–2.801, adjusted $p < .001$), and ventilation (OR 1.526, 95% CI 1.197–1.886, adjusted $p < .001$). Although univariate analysis indicated that patients with RD were more likely to undergoing tracheotomy (5.3% vs. 3.1%, $p = .012$), this was not significant when adjusting for demographic and hospital data on multivariable analysis (OR 1.540, 95% CI 0.934–2.522, $p = .088$).

4 | DISCUSSION

Multiple studies have demonstrated the strong correlation between RD and CLM.[4,11–14] Although the exact relationship between RD and CLM is debated, current literature suggests that as many as two-thirds of infants with CLM have RD.[11,13,14] Separate studies have found that RD might be associated with poorer outcomes and that neonates have poorer outcomes than older infants.[15,17,18] Using the 2016 KID, our study aims to provide a national perspective on the relationship between RD and CLM among a cohort of neonates.

Our cohort of 2212 neonates with CLM is, to our knowledge, the largest study to date directly investigating RD in CLM. Previously, a 2012 systematic review of CLM and acid reflux included a total of 1295 patients, with a 59% overall prevalence of RD.[14] Although most studies report a 35%–68% incidence of RD in infants with CLM, we report that only 26.45% of neonates with CLM had a diagnosis of RD.[11,13,14] This disparity in RD incidence might partially be attributed to our study only including neonates and their diagnoses by the time of discharge. Due to the nature of KID, we are unable to identify patients who were diagnosed with RD after discharge. Given that RD can present months after birth, this might account for the reduced incidence noted in our study.[14] For example, a study investigating CLM found differing rates of RD diagnoses between neonates (23%) and older infants (50%).[18]

Overall, our study indicates that RD is associated with poorer outcomes, higher charges, and increased need for intervention. Specifically, those with RD had greater total charges, longer LOS, more diagnoses on record, more procedures undergone, longer time until first procedure, increased odds for undergoing laryngoscopy, bronchoscopy, and ventilation. These results are generally consistent with existing literature demonstrating poorer outcomes in patients with RD.[15,17] One common explanation for these findings is that RD is a marker of severe CLM disease, so patients with RD are bound to have poorer outcomes.[17] However, others hypothesize that this relationship might be due to the fact RD alone is known to cause respiratory symptoms such as stridor, laryngeal irritation, exacerbation of subglottic stenosis, laryngospasm, and obstructive apnea.[20–22] Given these known associations, the compounding effect of CLM and RD may result in exacerbated symptoms and disease progression. Regardless, further studies are required to better understand the complex connection between RD and CLM.

Although most outcome markers demonstrated poorer results with RD, both mortality and odds for undergoing tracheotomy were similar between those with and without RD. Tracheotomy was previously the standard treatment for CLM and upper airway obstruction, but now it is rarely indicated.[4,23–26] Our univariate analysis demonstrated that RD patients had increased odds for undergoing tracheotomy, but this significance was lost on multivariable regression. The use of an even larger cohort might have prevented this loss of significance on analysis. Given that only 3.7% of patients in our cohort underwent a tracheotomy, it is likely that true differences were masked by the small incidence. A future study with an even larger cohort might provide increased clarity into if there is a real difference in tracheotomy rates between those with and without RD. Unlike tracheotomy, there was no significant difference in mortality on univariate analysis. Even though most of our outcome markers were poorer in the RD cohort, there are no differences in mortality. With increased attention on the medical management of CLM, even severe cases might have low mortality.[4,24] Furthermore, many severe cases might not result in death during the initial hospital stay but instead, lead to complex disease progression and increased future mortality.[18] Ultimately, even if mortality does not differ based on RD status, patients with RD clearly still have severer disease and poorer management.

The commonly accepted diagnostic tool for CLM is flexible fiberoptic laryngoscopy.[5–7] However, it is interesting to note that only 44.6% of patients with RD and 28.6% without RD underwent laryngoscopy during their hospital stays. Considering that our cohort only includes neonates, it is unlikely that these patients were diagnosed with CLM prior to their hospitalizations. This would indicate that most patients were diagnosed with CLM without undergoing a flexible fiberoptic laryngoscopy. Many case reports and series in existing literature only include CLM patients if they underwent a laryngoscopy to confirm the diagnosis.[4–8,17] Although not clearly indicated within the KID database, further information about the diagnostic methods for these patients would offer better insight.

Typically, the diagnosis of RD is made with pH testing and multichannel intraluminal impedance, or esophageal mucosal damage seen on endoscopy.[27–29] However, these testing guidelines are ever-changing, with new recommendations and guidelines provided frequently.[28] As a result, the diagnostic methods of RD are not standardized or uniform across providers and hospitals. In fact, a 2014 study highlighted these differences in the systematic overdiagnosis of RD.[30] However, it is unlikely that all RD diagnoses in our cohort are accurate. Considering these inconsistencies in RD diagnosis and the poorer outcomes of neonatal patients with RD in CLM, it might be prudent to increase RD testing in patients with severe CLM who are presenting with possible signs of reflux and gastrointestinal disease. Proper diagnosis could allow for the initiation of anti-reflux therapy, which might reduce symptoms and improve outcomes.[16]

Within RD, there are two major diagnoses included in our cohort: NER and GERD. The difference between the ICD-10 codes used to diagnose these is that NER is defined by reflux symptoms appearing within the first 28 days of life. Although these codes are similar, there might be differences noted in patients based on when they first presented with signs of RD. Carr et al. highlight differences in CLM presentation between neonates and older infants, and their findings are likely applicable to differences between NER and GERD as well.[18]

Even with the large sample size provided in KID, some limitations exist due to the retrospective nature of this study and the possibility of inconsistent and inaccurate ICD-10 coding. Specifically, the 2016 KID database did not include common comorbidity and complication data, as was done in past releases.[19] For example, our analysis did not account for neuromuscular diseases such as spinal muscular atrophy, congenital myasthenia gravis, and muscular dystrophy which have a strong correlation with CLM and RD. Although comorbidities and complication data can manually be extrapolated with ICD-10 codes, the lack of dedicated variables in KID may have resulted in the loss of valuable data and unmeasured confounding factors. Limitations in ICD-10 coding compared with other medical coding systems such as the Current Procedural Terminology prevented us from accurately identifying (1) differences in procedural modalities such as flexible and direct laryngoscopy and (2) patients undergoing surgical correction of LM such as supraglottoplasty. However, we examined the most common diagnoses and procedures within our cohort and within CLM literature to prevent omitting relevant information. As with any database, we are also limited by the information provided within KID and cannot account for errors with miscoding, missing variables, and misclassification. Analyses of KID are also limited to pediatric inpatients and our findings may not be generalizable to community CLM or laryngomalacia developing in children or adults. However, these factors are unlikely to impact the overall findings because of the large sample size afforded by this national database. Additionally, KID does not include longitudinal data for patients after discharge. If this data were included, it would likely strengthen our findings and provide additional insight into differences in CLM based on RD status.

Our findings should be carefully considered within the context of these limitations, but additional analysis would, likely, strengthen our findings. Given our cohort size and the generalizability of KID, we

believe that our results can be applied from a national perspective. Further studies including even greater sample sizes, longitudinal data, and more comorbidity and complication data will likely provide detailed insights into the specific associations of RD with CLM in neonates.

CONCLUSION

Our study provides a national perspective of RD (i.e., GERD and NER) in neonates admitted to the hospital with a diagnosis of CLM, the most common cause of stridor in neonates and laryngeal anomaly in newborns. Compared to those without RD, patients with RD had greater total charges, longer LOS, more diagnoses on record, more procedures undergone, longer time until first procedure, increased odds for undergoing laryngoscopy, bronchoscopy, and ventilation, but similar odds for mortality and undergoing a tracheotomy. Given these findings, testing for RD might be indicated in patients with CLM presenting with severe disease or signs of reflux. Further studies are required to elucidate the cause-and-effect relationship between RD and CLM.

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CONFLICT OF INTEREST STATEMENT

The authors report no conflicts of interest.

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REFERENCES

1. Holinger LD. Etiology of stridor in the neonate, infant and child. *Ann Otol Rhinol Laryngol*. 1980;89(5 Pt 1):397-400.
2. Thomson J, Turner AL. On the causation of the congenital stridor of infants. *Br Med J*. 1900;2(2083):1561-1563.
3. Cohen O, Picard E, Joseph L, Schwartz Y, Sichel JY, Attal P. Supraglottoplasty for severe laryngomalacia. Can we predict success? *Int J Pediatr Otorhinolaryngol*. 2020;138:110333.
4. Olney DR, Greinwald JH Jr, Smith RJ, Bauman NM. Laryngomalacia and its treatment. *Laryngoscope*. 1999;109(11):1770-1775.
5. Ayari S, Aubertin G, Girschig H, Van Den Abbeele T, Mondain M. Pathophysiology and diagnostic approach to laryngomalacia in infants. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2012;129(5):257-263.
6. Macfarlane PI, Olinsky A, Phelan PD. Proximal airway function 8 to 16 years after laryngomalacia: follow-up using flow-volume loop studies. *J Pediatr*. 1985;107(2):216-218.
7. Thompson DM. Abnormal sensorimotor integrative function of the larynx in congenital laryngomalacia: a new theory of etiology. *Laryngoscope*. 2007;117(6 Pt 2 Suppl 114):1-33.
8. Faria J, Behar P. Medical and surgical management of congenital laryngomalacia: a case–control study. *Otolaryngol Head Neck Surg*. 2014;151(5):845-851.
9. Manning SC, Inglis AF, Mouzakes J, Carron J, Perkins JA. Laryngeal anatomic differences in pediatric patients with severe laryngomalacia. *Arch Otolaryngol Head Neck Surg*. 2005;131(4):340-343.
10. Belmont JR, Grundfast K. Congenital laryngeal stridor (laryngomalacia): etiologic factors and associated disorders. *Ann Otol Rhinol Laryngol*. 1984;93(5 Pt 1):430-437.
11. Nussbaum E, Maggi JC. Laryngomalacia in children. *Chest*. 1990;98(4):942-944.
12. Luebke K, Samuels TL, Chelius TH, et al. Pepsin as a biomarker for laryngopharyngeal reflux in children with laryngomalacia. *Laryngoscope*. 2017;127(10):2413-2417.
13. Roger G, Denoyelle F, Triglia JM, Garabedian EN. Severe laryngomalacia: surgical indications and results in 115 patients. *Laryngoscope*. 1995;105(10):1111-1117.
14. Hartl TT, Chadha NK. A systematic review of laryngomalacia and acid reflux. *Otolaryngol Head Neck Surg*. 2012;147(4):619-626.
15. Bibi H, Khvolis E, Shoseyov D, et al. The prevalence of gastroesophageal reflux in children with tracheomalacia and laryngomalacia. *Chest*. 2001;119(2):409-413.
16. Apps JR, Flint JD, Wacogne I. Does anti-reflux therapy improve symptoms in infants with laryngomalacia? *Arch Dis Child*. 2012;97(4):385-387. discussion 387.
17. Giannoni C, Sulek M, Friedman EM, Duncan NO 3rd. Gastroesophageal reflux association with laryngomalacia: a prospective study. *Int J Pediatr Otorhinolaryngol*. 1998;43(1):11-20.
18. Carr MM, Ramadan J, Bauer E. Laryngomalacia in neonates versus older infants: HCUP-KID perspective. *Clin Pediatr (Phila)*. 2020;59(7):679-685.
19. Introduction To The HCUP KIDS' Inpatient Database (KID). Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project (HCUP). 2016 https://www.hcup-us.ahrq.gov/db/nation/kid/KID_2016_Introduction.pdf. Published September 2018. Accessed
20. Burton DM, Pransky SM, Katz RM, Kearns DB, Seid AB. Pediatric airway manifestations of gastroesophageal reflux. *Ann Otol Rhinol Laryngol*. 1992;101(9):742-749.
21. Nordenstedt H, Nilsson M, Johansson S, et al. The relation between gastroesophageal reflux and respiratory symptoms in a population-based study: the Nord-Trøndelag health survey. *Chest*. 2006;129(4):1051-1056.
22. Wenzl TG, Silny J, Schenke S, Peschgens T, Heimann G, Skopnik H. Gastroesophageal reflux and respiratory phenomena in infants: status of the intraluminal impedance technique. *J Pediatr Gastroenterol Nutr*. 1999;28(4):423-428.
23. Glenn WW, Gee JB, Cole DR, Farmer WC, Shaw RK, Beckman CB. Combined central alveolar hypoventilation and upper airway obstruction. Treatment by tracheostomy and diaphragm pacing. *Am J Med*. 1978;64(1):50-60.
24. Baljosevic I, Minic P, Trajkovic G, Markovic-Sovtic G, Radojicic B, Sovtic A. Surgical treatment of severe laryngomalacia: six month follow up. *Pediatr Int*. 2015;57(6):1159-1163.
25. Zalzal GH, Anon JB, Cotton RT. Epiglottoplasty for the treatment of laryngomalacia. *Ann Otol Rhinol Laryngol*. 1987;96(1 Pt 1):72-76.
26. Solomons NB, Prescott CA. Laryngomalacia. A review and the surgical management for severe cases. *Int J Pediatr Otorhinolaryngol*. 1987;13(1):31-39.
27. Vaezi MF, Choksi Y. Mucosal impedance: a new way to diagnose reflux disease and how it could change your practice. *Am J Gastroenterol*. 2017;112(1):4-7.
28. Vaezi MF, Pandolfino JE, Vela MF, Shaheen NJ. White paper AGA: optimal strategies to define and diagnose gastroesophageal reflux disease. *Clin Gastroenterol Hepatol*. 2017;15(8):1162-1172.

29. Wang WH, Huang JQ, Zheng GF, et al. Is proton pump inhibitor testing an effective approach to diagnose gastroesophageal reflux disease in patients with noncardiac chest pain?: A meta-analysis. *Arch Intern Med*. 2005;165(11):1222-1228.
30. Pleyer C, Bittner H, Locke GR 3rd, et al. Overdiagnosis of gastroesophageal reflux disease and underdiagnosis of functional dyspepsia in a USA community. *Neurogastroenterol Motil*. 2014;26(8):1163-1171.

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