INFANT VOCAL CORD PARALYSIS:
A POPULATION-BASED PERSPECTIVE

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ABSTRACT

Objectives/Hypothesis: Infantile vocal cord paralysis (VCP) is an uncommon but potentially dangerous condition with a significant potential for both short and long-term deleterious sequelae. Our objectives were to utilize a population-based resource to characterize hospitalized children with VCP. Furthermore, we compare these characteristics between live born infants and infants subsequently readmitted and discharged with VCP.

Study Design: Cross Sectional Study of Pediatric Hospital Admission during the years 2006, 2009, and 2012.

Methods: The study examined inpatient admissions for pediatric patients with VC Pusing the Kids´ Inpatient Database (KID), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality. Infants (age ≤ 3 years old) with VCP were characterized with respect to demographics and outcomes.

Results: An estimated 8,527 (0.06%) infants were diagnosed with VCP during their hospitalization. Of these hospitalizations, 10.1% were live born. The majority was male (52%) and Caucasian (51%). Unilateral VCP was most common (51.5%). Patients with VCP were significantly more likely to have associated intrauterine and birth co-morbidities. Concurrent neurologic and cardiac congenital anomalies were also more common. Tracheostomy was more common, even among newborns with unilateral immobility.

Conclusions: VCP is one of the most common causes of pediatric airway obstruction. Patients identified at birth have worse outcomes, specifically in terms of intubation requirements and more complicated hospital courses, compared to those diagnosed on subsequent hospitalizations. Continued inquiry into natural history, particularly among newborns, is indicated

INTRODUCTION

Vocal cord paralysis (VCP) during infancy engenders a variety of sequelae harboring a wide range of impact on quality of life and even survival. Clinical presentation may be influenced by numerous factors including whether a lesion is unilateral or bilateral, age of presentation, and underlying etiology. [1-4] For example, infants with bilateral VCP may present with stridor and respiratory difficulties necessitating airway control with an endotracheal intubation or tracheotomy. These interventions are also not without risk having negative potential consequences of their own. [5-8] It must also be kept in mind that there is no definitive consensus identifying predictive markers and the possibility of spontaneous recovery of nerve function is a distinct possibility. [4]

In contrast to bilateral VCP, unilateral VCP tends to present with noisy breathing and feeding difficulty [9, 10] rather than respiratory distress. For those who do not recover spontaneously, there are several management strategies that may be useful in facilitating rehabilitation but timing of interventions is still debated. Strategies for management include but are not limited to speech therapy, vocal cord medialization, and other surgical approaches such as re-innervation procedures. [10]

Although the therapeutic repertoire for managing infant VCP has expanded considerably in recent years, [5, 10-14] many questions remain regarding prognostic and associated factors among these patients despite numerous case series and reviews of the literature examining this topic. Our primary objective was to utilize the KID Database to examine the characteristics of hospitalized infants diagnosed with VCP in the United States. The KID is largest all payer pediatric inpatient database in the United States and via it's complex survey designs can estimated up to 7 million pediatric discharges per release year. This attribute makes it suitable to study rare conditions like pediatric vocal cord paralysis. This resource has demonstrated its unique value in prior analyses, [15-18] as it allows for examination of population-based data that lends greater external validity to findings relative to smaller intra-institutional chart reviews.

METHODS

The authors sampled the Kid's Inpatient Database (KID), Healthcare Cost and Utilization Project (HCUP), and Agency for Healthcare Research and Quality (AHRQ) using data from three separate release years (2006, 2009, and 2012). As mentioned, it is the largest all-payer database detailing U.S. pediatric inpatient admissions, this resource details clinical information that can be used to estimate up to 7 million discharges each year as well as examining discharges from approximately 3000 – 4000 community hospitals located in 44 separate states. [17, 19]

We examined this database for infants – defined as children 3 years of age and younger with diagnoses encompassing vocal cord immobility utilizing the ICD9-CM codes 478.30 (VCP, not otherwise specified), 478.31

(unilateral VCP), and 478.34 (bilateral VCP). We further divided the patients into "newborns." Newborn infants were identified by ICD-9 codes indicating live born status during their hospitalization. Variables were examined with respect to demographics, associated diagnoses, procedures performed, length of stay, presence of complications, and mortality. Additionally, we examined for the presence or absence of intrauterine growth retardation (IUGR), hypoxia, respiratory distress syndrome (RDS), birth trauma, low birth weight (< 2500 g) very low birth weight (< 1500 g), cardiac, GI, neurological, and other congenital conditions. Infants with VCP were compared to all infants (children ≤ 3 years of age) discharged in the KID database during the same study period. ICD-9 Codes utilized for this project are noted in **Table 1**.

Table 1: ICD-9 Codes.

Code	Description
478.30	Vocal cord paresis
478.31	Unilateral paralysis of vocal cord or larynx, partial
478.32	Unilateral paralysis of vocal cord or larynx, complete
478.33	Bilateral paralysis of vocal cord or larynx, partial
478.34	Bilateral, paralysis of vocal cord or larynx, complete

Statistical Analysis

The KID Database uses a complex survey design with statistical weighting to estimate national discharges. We used Taylor series linearization to produce the estimations of discharges. Post-estimation analysis included calculation of means and proportions with standard errors and 95% confidence intervals of continuous and categorical data where applicable. We also constructed simple linear and logistic regression models to examine for difference between patient with and without vocal cord paralysis. Multiple regression analysis was done to look for cofounding between male gender and newborn status. The observation-weighted grand mean of the variable of interest was baseline value for regression model comparisons. Due to overlap in ICD9-CM codes for neonatal conditions as well as the large sample size, statistical significance was set at p ≤ 0.01. All statistics were should done with StataCorp. 2015. *Stata Statistical Software: Release 14*. College Station, TX: StataCorp LP.

RESULTS

Baseline characteristics are presented in Table 2. An estimated 8,526 (95% CI, 8301 – 8751) discharges were associated with a diagnosis of vocal cord paralysis (NOS, unilateral, or bilateral) of which 860 were newborn, which amounted to 7.2 cases for every 100,000 newborns in the KID Database for the study years. Unilateral was the most common diagnosis (51.2%) followed by VCP-NOS (30%) and bilateral (18.6%). The mean age was 10 months. The majority was male (55%) and the most common ethnicity was White (51.1%) followed by Hispanic (23%). Patients with any diagnosis of vocal paralysis were slightly more likely to be male (OR 1.05, p<0.01) and

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Hispanic (OR 1.11, p<0.01). In contrast, females (0.94, p<0.01), Asians (0.78, p<0.01), and Whites (0.93, p< 0.01) were less like to have any vocal cord paralysis. Hospitalized infants with vocal cord paralysis were also older compared to the entire cohort of hospitalized infants (10.1 months vs. 2.7 months, p < 0.01). The distribution of paralysis types (NOS, unilateral, and bilateral) was similar for each ethnic group (White, Black, Hispanic, et al; p = 0.67) (**Table 3**).

Table 3. Racial Breakdown of Patients (%).

	C	**AA**	**His**	**Asn**	**Nat**	**Other**
Unilateral	47.6	14.6	25.3	3.4	1.2	7.9
Bilateral	47.7	14.4	25.8	4.3	0.4	7.4
NOS	46.9	14.9	25.7	3.3	0.7	8.4

NOS = not otherwise specified. C = Caucasian, AA = African American,

His = Hispanic, Asn = Asian, Nat = Native American / Pacific Islander

Newborns with VCP had a significantly higher likelihood of requiring intubation (p < 0.01) as well as tracheostomy (p < 0.01) than age-matched controls. The intubation rate was 9.3% and tracheostomy rate was 7.1% for infants with vocal cord paralysis.

Newborns and infants diagnosed with bilateral VCP had a higher likelihood of having congenital nervous system anomalies (p < 0.01) (**Figure 1**). Furthermore, infants with unilateral VCP had a higher likelihood of having cardiac congenital anomalies (p <0.01). Analysis by associated co-morbidities/conditions organized by type of paralysis is illustrated in **Figure 2**.

DISCUSSION

The general consensus has been that laryngomalacia is the most common laryngeal etiology for stridor in infants. [20, 21] Nonetheless, our analysis utilizing a nationally representative dataset revealed a 0.7% incidence of vocal cord paralysis among hospitalized infants. To our knowledge, this is the first study to determine the incidence of infant vocal cord paralysis in the infant population.

Management approaches to unilateral and bilateral VCP differ depending on several factors, including age at presentation and severity of symptoms. [3,4,10,14,17,22-24] As patients with bilateral VCP present with potentially more serious airway sequelae and respiratory distress than those with unilateral VCP, practitioners may have a lower threshold for definitive airway management. Alternative strategies may include observation if patient condition permits, non-invasive positive pressure ventilation, and cordotomy procedures.[4] Additionally, airway procedures including arytenoidectomy, laryngoplasty, and even nerve reinnervation have been explored by other groups with varying success.[4,11-13,25-27] Despite these commonly taught management principles heavily detailed in the literature, our sample of 8,527 infants did not find a statistically significant increased likelihood of tracheotomy in unilateral VCP patients compared to age and disease matched controls. This may be due to the fact that unilateral vocal cord paralysis does not necessarily require a tracheostomy for airway protection. Nonetheless, we did note a

significantly increased likelihood of intubation in newborns diagnosed with VCP, both in the unilateral and bilateral VCP cohorts (**Figure 1**) (p-values < 0.01).
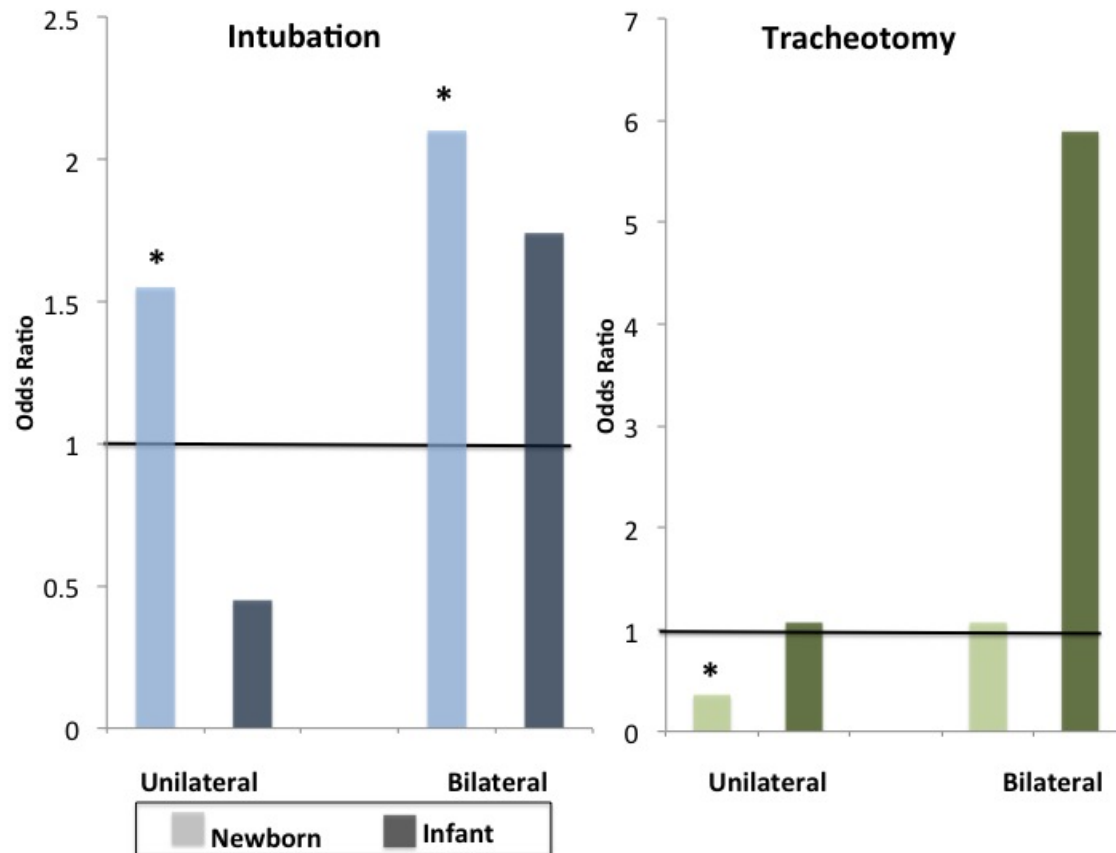
Figure 1. Likelihood of Airway Intervention. Light (left) bars represent newborn patients, right (dark) bars represent infant patients. Asterisks denote statistical significance (p < 0.01) of Odds ratio. Horizontal dark line represents Odds ratio of 1.

Upon examination by associated co-morbidities, unilateral lesions tended to be more common than bilateral VCP (**Figure 2**). An important exception was found among infants with associated nervous system congenital anomalies, where 36.4% of patients were found to have bilateral VCP while 29.1% had unilateral VCP. This finding emphasizes the importance of aggressively looking for other neurologic lesions in children presenting with bilateral VCP, and having a low threshold for pursuing central nervous system imaging such as an MRI to rule out associated anomalies, such as an Arnold-Chiari malformation. [1]
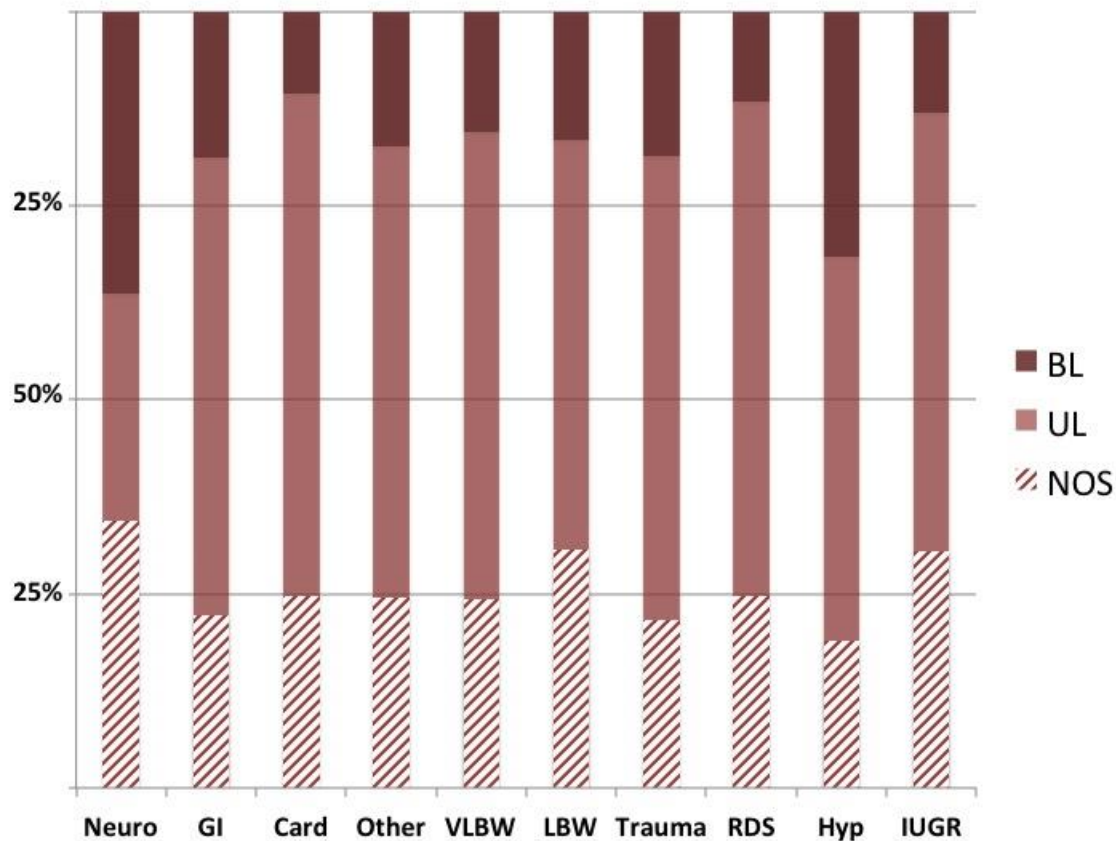
Figure 2. Type of vocal cord paralysis organized by co-morbidity. U/L = Unilateral, B/L = bilateral. IUGR = Intrauterine growth retardation, Hyp = Intrauterine hypoxia and birth asphyxia, RDS = respiratory distress syndrome, Trm = trauma, LBW = low birth weight, Card = cardiac, GI = Digestive congenital anomalies, Other = other perinatal conditions, N = Nervous congenital anomalies

Hypoxia, congenital heart disease, and gastrointestinal anomalies were more common in all infants with VCP (**Table 2**). Furthermore, congenital cardiac anomalies appeared to be more common in infants with VCP diagnosed on a later hospitalization rather than as a newborn. This latter finding is likely a result of patients presenting with iatrogenic injury following cardiac surgery, as recurrent laryngeal nerve and/or vagus injury is a known risk of congenital cardiac surgery.[28, 29] Importantly, this emphasizes the importance for practitioners involved in the care of infants undergoing heart surgery to include VCP in a comprehensive pre-operative informed consent process, and possibly collaborating with a pediatric otolaryngologist pre-operatively in cases where there may be a high risk of such complications.

Table 2. Likelihood of Associated Co-Morbidity (Expressed as an Odds Ratio).

Type	IUGR	Hyp	RDS	Trm	LBW	VLBW	Card	GI	Other	N
Newborn U/L	0.81	0.4	0.52	0.51	1.1	1.76	0.55	1.13	0.72	1.55
Newborn B/L	0.96	0.23	0.63	0.39	1.8	11.2	0.64	1.24	1.22	2.10*
Infant U/L	0.96	1.71	1.65	0.44	0.8	0.92	**2.27***	1.52	1.63	0.45
Infant B/L	0.6	3.23	0.85	0.56	0.64	0.22	0.59	1.35	1.22	1.74*

Results with an asterisk (*) and **bolded** represent statistically significant comparisons ($p < 0.01$).

U/L = Unilateral, B/L = bilateral. IUGR = Intrauterine growth retardation, Hyp = Intrauterine hypoxia and birth asphyxia, RDS = respiratory distress syndrome, Trm = trauma, LBW = low birth weight, Card = cardiac, GI = Digestive congenital anomalies, Other = other perinatal conditions, N = Nervous congenital anomalies.

Although in many instances spontaneous return of vocal cord mobility may occur, many infants with VCP require significant rehabilitation and may experience deleterious chronic and even lifelong sequelae of which parents should be aware. Furthermore, parents may need to be counseled on both established and emerging therapeutic alternatives to tracheotomy, including the surgical procedures detailed above. Hence, as perceived inadequacies in informed consent were a common allegation, comprehensive discussion of risks, alternatives, and benefits, as well as appropriate documentation of this discussion could improve parents understanding of VCP and potentially minimize liability in such a situation.

Although there are numerous advantages to analyzing data from a nationwide resource such as the KIDS database, there are several limitations inherent to its use. While this database offers an excellent opportunity to evaluate trends from a population-based perspective, detailed clinical characteristics of individual cases are not available, demonstrating the complementary value of existing intra-institutional studies examining VCP. Hence, this resource utilizes discrete data points and does not have these specifics as well as other important considerations such as clinical course. Nonetheless, single and even multi-institution studies that are reported in the literature have nowhere near the sample size examined in the current analysis, allowing the findings we do report in this manuscript a far greater degree of external validity. Importantly, utilization of population-based resources such as the KID database is an important complement to rather than replacement for the available literature on this subject.

CONCLUSIONS

Vocal cord paralysis, although rare, is still one of the most common causes of pediatric airway obstruction, with an estimated incidence of 0.07% reported using the KIDs database. This is the first study to determine the incidence of vocal cord paralysis in the infant population. Although most cases are not identified at birth, this analysis demonstrates that newborn infants with vocal cord paralysis are more likely to have certain comorbidities, and subsequently, a more complicated inpatient course. Newborns with vocal cord paralysis are significantly more likely to require intubation, with a potential for increased sequelae down the line from this. Additionally, patients presenting with vocal cord paralysis at birth have worse outcomes and a more complicated hospital course compared to those diagnosed on subsequent hospitalizations.

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