

Upper-Lip Frenum as a Predictive Marker for Unexpected and Unexplained Asphyxia in Infants

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Received: February 18, 2016; **Accepted:** March 03, 2016; **Published:** March 10, 2016

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Citation: Haller LA, Brown T. Upper-lip Frenum as a Predictive Marker for Unexpected and Unexplained Asphyxia in Infants. J Rare Dis Diagn Ther. 2016, 2:2.

Abstract

Objective: To determine if there is a relationship between restricted upper-lip frenums (upper lip ties) and unexpected and unexplained asphyxia (UUA) in infants.

Methods: A retrospective review was done of 327 UUA cases from Miami-Dade County, FL and Harris County, TX. Using autopsy photos, upper-lip frenums were classified by degree of restriction. Statistical analysis was done to compare the occurrence of restricted upper-lip frenums in this UUA population to a baseline for the general population. The difference was statistically significant at the 99% confidence level.

Conclusion: There is a very strong statistical correlation between restricted upper-lip frenums and UUA infant deaths.

Keywords: Frenum; Frenectomy; Tongue-tie; Ankyloglossia; Lip-tie; Unexpected and unexplained asphyxia; Sudden infant death syndrome; Sudden unexpected infant death

Abbreviations

UUA: Unexpected and Unexplained Asphyxia; SIDS: Sudden Infant Death Syndrome; SUID: Sudden Unexpected Infant Death

Introduction

Unexpected and unexplained asphyxia (UUA), often referred to in the literature as Sudden Infant Death Syndrome (SIDS), remains the leading cause of death in infants from 1 to 12 months old [1]. Much effort has been put into discovering the causes and working toward prevention of this phenomenon. Researchers agree that there are both internal (infant biological vulnerability) and external (environment) risk factors that are seen in this population in various combinations and to

various degrees [2]. Of the infant vulnerability risk factors that have been identified, prematurity and congenital, maturational, or acquired brainstem dysfunction fit with a model of immature formation of biological functions [3]. We postulate that ankyloglossia (tongue-tie) and restricted upper-lip frenums (lip-tie) might be another of the maturational biologic vulnerabilities that contribute to UUA.

The populations of UUA infants and infants with tongue-ties have several similarities. They both occur more frequently in males than in females by a ratio of approximately 3:1 and can have a genetic component. Reporting of incidence of these populations varies, but they both occur in approximately 5% of the general population [4, 5].

There is also a correlation between successful breastfeeding and reduced risk of UUA [6]. Tongue-ties and upper lip ties have been shown to significantly interfere with an infant's ability to breastfeed [7-12]. It may be that rather than breastfeeding being protective for UUA, the inability to breastfeed may be a risk factor.

The oral cavity forms from all three primary germ layers, ectoderm, mesoderm and endoderm. In most cases, the ectoderm resorbs leaving only small residual web-like tissue connections between the tongue and the floor of the mouth and between the lips and the maxillary and mandibular ridges. These are called frenums. In some cases, the ectoderm does not resorb completely, leaving frenums that are tight and that restrict movement of the tongue (ankyloglossia or tongue-tie) and lips (lip-tie).

Infants depend on a suck-swallow-breath mechanism that is facilitated by using flanging of the lips around the breast to create a seal for sucking and using the back of the tongue to latch onto the nipple and actively squeeze milk from the breast into the oral cavity for swallowing [7]. This mechanism is more difficult for infants with tongue and upper-lip ties. They frequently have low or no weight gain due to not receiving adequate nutrition. They also tend to ingest air into their stomachs and to regurgitate stomach contents through their noses and mouths [13]. These infants are frequently described as "fussy" because they are always hungry and suffering from gas pain and reflux.

Infants also use the back and mid tongue to modulate the opening between lungs and GI tract. If an infant's tongue is pulled forward by a tight frenum that is anchoring the tongue, the infant must actively work to push the tongue back to keep from inhaling regurgitated stomach contents. This would explain why placing infants on their backs have been helpful in reducing the incidence of UUA. When supine, gravity helps pull the tongue back. When prone, the infant must work to push the tongue back. Once the infant falls asleep, the infant no longer actively works to maintain the airway enabling regurgitated stomach contents to be inhaled leading to asphyxia. This would also explain why, at autopsy, stomach contents are frequently found in airways of UUA infants, although this has been attributed to agonal changes [14-16].

Tongue-ties can be difficult to diagnose. Many are obvious, but others are deep under the tongue (termed submucosal) and appear normal even though they are restricting tongue movement in the posterior area that is so crucial for breastfeeding. The only way to accurately diagnose a submucosal tongue-tie is to carefully evaluate the infant's tongue function [7, 9, 10]. This can be a challenge. However, the same incomplete resorption that causes a tongue-tie also causes an upper-lip tie. In fact, a tongue-tie usually, if not always, exists whenever there is an upper-lip tie [10, 17]. Fortunately, upper-lip ties can be easily evaluated by simply retracting the upper lip and looking at where the tissue inserts with respect to the maxillary ridge. If an infant is having difficulty breastfeeding and a tongue-tie is not obvious, evaluating the upper-lip frenum can help alert the clinician to the existence of a possible submucosal tongue-tie. Both upper-lip and tongue-ties (even submucosal ones) can be safely corrected through a simple frenectomy procedure.

The hypothesis for this study is that if tongue and upper-lip ties are contributors to UUA, and if upper-lip ties occur concurrently with tongue-ties, then we should see a higher frequency of upper-lip ties in UUA cases than in the general population. If so, then the simple evaluation of an upper-lip tie by medical and lactation professionals would be an easy and effective way to identify infants at risk of UUA.

Methods

To test the strength of the hypothesis that there is a relationship between easily observable upper-lip ties and UUA, we reviewed autopsy photos of upper-lip frenums for all infants up to age 730 days old between 2009 and 2015 in Miami-Dade County, Miami, FL and between 2012 and 2015 in Harris County, Houston, TX. The upper-lip frenum for each de-identified case (photos were identified by case number only) was evaluated using the Kotlow classification system shown in **Figure 1** [11]. This system grades upper-lip frenums by degree of tightness based on where the attachment is located with respect to the maxillary ridge.

Class I is completely unrestrictive because the frenum attaches to the movable gingiva well above the maxillary ridge.

Class II is slightly tight but still not restrictive because it extends low enough to attach to the unmovable gingival tissue but still well above the crest of the maxillary ridge. Class III is very tight because it attaches at the crest of the maxillary ridge. And Class IV is extremely tight and restrictive because it attaches at the crest of the maxillary ridge and wraps around the ridge towards the palate. For this analysis, the cases were grouped into two categories: Unrestrictive (Classes I and II) and Restrictive (Classes III and IV). To prevent evaluator bias, evaluation was done on all cases with no knowledge of cause of death.

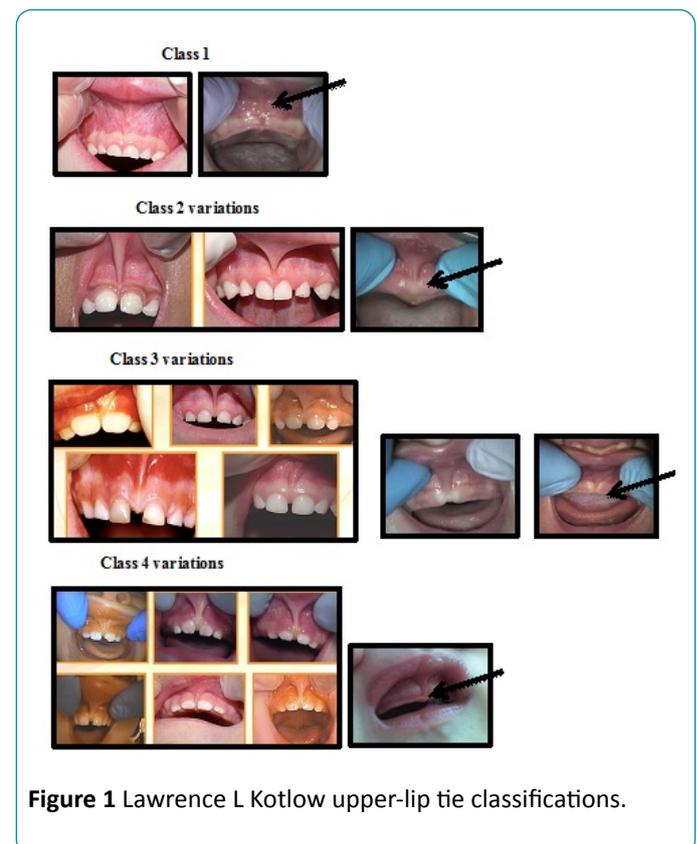


Figure 1 Lawrence L Kotlow upper-lip tie classifications.

There is inconsistency in the cause of death recorded by medical examiners for infants who die unexpectedly without an obvious cause or explanation. Since 1969, the term SIDS has been used. Over the years that term has come under criticism, but with no agreement on what to substitute for it [2]. Therefore, these cases of asphyxia have been recorded as, among other things, SIDS, Unknown, Undetermined, Co-sleeping, Overlay, Asphyxia, SUID (Sudden Unexpected Infant Death), and ASSB (Accidental Suffocation and Strangulation in Bed). Based on the cause of death assigned by the medical examiners, each case was coded as UUA or Other. The UUA group included cases with cause of death SIDS, Unknown, Undetermined, Co-sleeping, Overlay, Asphyxia, or SUID. All other cases, including Pneumonia, Sepsis, Complications of Prematurity, Asthma, Trauma, Congenital Anomalies and Homicide were coded as other. Pending cases and cases with no autopsy photo were also not included. Only the UUA cases were used for this analysis.

Results

Summary data

The total number of UUA cases was 327. **Figure 2** shows summary data by gender. The ratio of males to females is 75% or 3:2 which is consistent with other research from the general population [5].

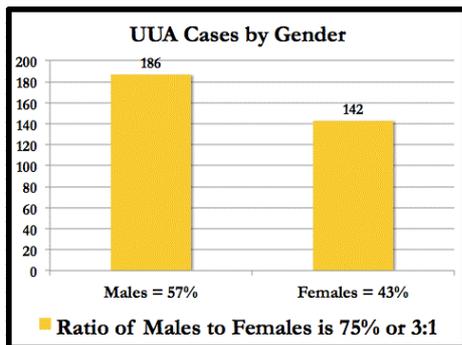


Figure 2 UUA cases by gender.

Figure 3 shows summary data by race with 48% white, 29% Black, 21% Hispanic, 1% Asian and 1% other. **Figure 4** shows UUA deaths by age at death with 84.5% occurring within the first 6 months of life; and 50.5% of those occurring within the first 2 months of life. This is also consistent with the literature [18].

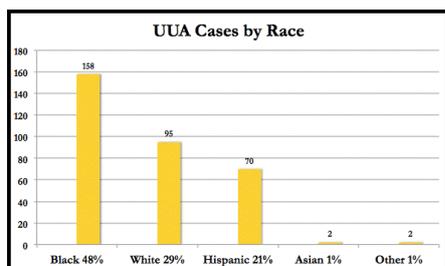


Figure 3 UUA cases by race.

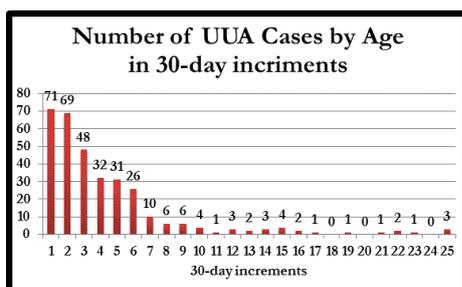


Figure 4 UUA cases by age at death in 30 day increments.

Statistical analysis

Figure 5 shows the number of restricted and unrestricted frenums among the UUA cases: 84% restricted, 16% unrestricted.

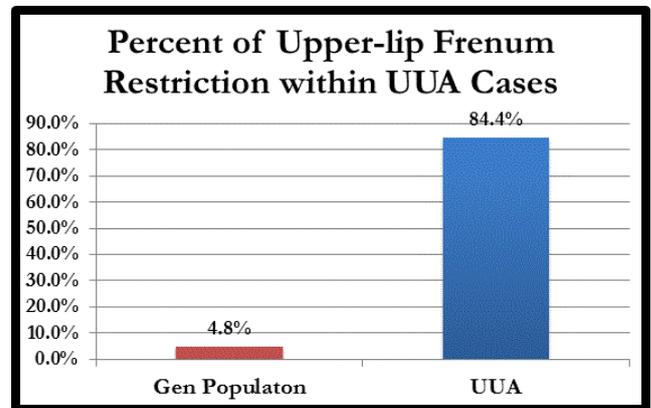


Figure 5 Restricted and unrestricted upper-lip frenums for UUA cases.

To statistically test our hypothesis that there are more restricted frenums in the UUA population than in the general population, we used a single-group t-test. For this t-test we needed a baseline percentage of occurrences for the general population. **Table 1** [19-22] shows a sampling of articles reporting incidence of tongue-ties. There is insufficient information on the occurrence of upper-lip ties in the general population. However, because tongue-ties are usually, if not always, found when there is an upper-lip tie, we used the incidence of tongue-ties reported in the literature as a proxy for incidence of upper-lip ties [17]. If this introduces any bias into our analysis, it is to overestimate the incidence of upper-lip ties in the general population and thus to cause us to underestimate any association that may exist with UUA.

The reported incidence of tongue-ties is from 2.3 to 16.4 percent. The generally accepted value is somewhere in the range of 2.0-4.8. In contrast, **Figure 6** shows that 84% of the infants in our sample had a restricted upper-lip frenum. The single-group t-test statistic for comparison of upper-lip ties in our cases versus a baseline of 4.8% is significant at the 99% confidence level. It is also significant at the 99% confidence level when compared to a baseline of 16% (**Table 2**).

Discussion and Limitations

The results of this study reveal a strong relationship between the existence of restricted upper-lip frenums and UUA. Therefore, the presence of an upper-lip tie can be used by pediatricians and other medical professionals as a diagnostic tool for identifying children at risk for UUA.

The fact that our data is retrospective is a significant limitation of this study. The infants are post mortem with incomplete information about the symptoms of tongue and

upper-lip ties. This lack of a medical history that includes difficulty breastfeeding, GI reflux, gas pain, slow or no weight-gain, whether or not a frenectomy procedure was performed prior to death, as well as other possible confounding factors, prevents us from drawing conclusions regarding causation.

Perhaps the relationship between upper-lip frenums and UUA reflects that both are the result of prematurity or low birth weight [22-26]. For example, multiple researchers have discovered that premature infants with low birth weight have increased cardiovascular risk [22, 26]. This could be a cause of UUA deaths that may or may not be related to the high frequency of frenums in that population.

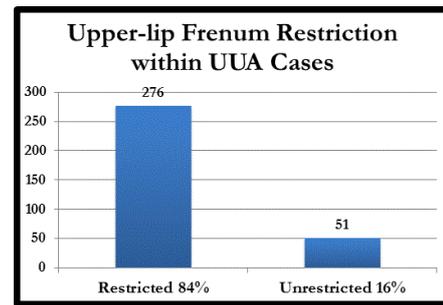


Figure 6 Percent of upper-lip frenums restricted, UUA cases.

Table 1 Table of publications and reported incidence of tongue-ties.

Author and Publication	Population	Percent Reported
Buryk M, Bloom D, Sophie T and Efficacy of Neonatal Release of Ankyloglossia [19].	Randomized, single-blind study on neonates with breastfeeding issues	1.7 to 4.8
Ricke LA, Baker NJ, Madlon-Kay DJ, DeFor TA and Newborn Tongue-tie: Prevalence and Effect on Breastfeeding [20].	All infants in a regional hospital examined to determine incidence of tongue-ties	4.2
Pavithra M, Vaz AC and Ankyloglossia Among Children of Regular and Special Schools in Karnataka, India: A Prevalence Study [21].	700 children ages 9 – 17 examined for tongue-ties	16.4
Hogan M, Westcott C, Griffiths M and Randomized, controlled trial of division of tongue-tie in infants with feeding problems [22].	201 babies in South Hampton with breastfeeding problems	10.7

Table 2 Results of t-test for combined Miami-Dade and Harris County data using Excel StatPlus.

One-Sample T-Test									
	Mean	Mean LCL	Mean UCL	Standard Error	Sample size	Hypothesized value	Difference	Test Statistics	d.f.
UUA	0.84498	0.79827	0.8917	0.01998	329	0.048	0.79698	39.88186	328
One-Sample T-Test									
	Mean	Mean LCL	Mean UCL	Standard Error	Sample size	Hypothesized value	Difference	Test Statistics	d.f.
UUA	0.84498	0.79827	0.8917	0.01998	329	0.16	0.68498	34.27727	328

Cortese et al. found increased risk for infection in premature infants with low birth weight [26]. The clinical symptoms they identify as being helpful in making the difficult diagnosis of infection in infants include: delayed weight gain, anorexia, regurgitation, abdominal distension and vomiting. They report risk factors of, among other things, prematurity, male gender and anemia. These clinical symptoms and risk factors are remarkably similar to clinical presentations and risk factors for infants with tongue and upper-lip ties. Although we explicitly excluded from our sample infant deaths caused by cardiovascular problems, pneumonia or sepsis, it could be possible that the correlation between restricted frenums and UUA deaths reflects a failure by forensic pathologists to accurately identify one or both of these other causes resulting in misidentification as UUA.

Still, the strong correlation identified in our study is consistent with the possibility of a causal relationship between

restricted frenums and UUA. Confirmation or refutation of a causal relationship would require a prospective, hospital-based matched case-controlled study.

Conclusion

This paper found a very strong correlation between the existence of restricted upper-lip frenums and UUA. At minimum, these results imply that medical professionals should adopt the practice of evaluating upper-lip frenums to identify infants at high risk of UUA. Whether the relationship between restricted frenums and UUA is causal or simply an indirect association remains an open question requiring further research. However, with current research showing the safety, effectiveness, and simplicity of laser-assisted frenectomies even in infants only a few days old [27-29], and with the majority of UUA deaths occurring within the first few

months of life, pediatricians should consider the possibility that treating restricted frenums within the first few months of life would now be prudent.

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