

# Scoping literature review: gastrointestinal signs in infants with ankyloglossia

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**Background:** Improvement of reported gastrointestinal (GI) signs are used to prove efficacy of ankyloglossia correction. The aim of this scoping review was to summarize GI signs observed in infants with restricted tongue mobility known as ankyloglossia, or tongue tie, through the discussion of relevant quantitative data of associated GI signs. Although common in infancy, reflux is one of the relevant signs discussed in this review.

**Methods:** PubMed and CINAHL were used for this scoping review that resulted in a total of 132 articles with 17 repeated articles between the two searches. Inclusion criteria were infants from birth to 23 months, written in the English language, and relevant peer-reviewed research articles. Articles were excluded if not original research, research that did not address GI signs, qualitative research, if children were older than 23 months, or if written in another language. All articles from inception to the date of the search on March 31, 2023, were considered. Out of the 115 reviewed articles, seven were included and manually referenced in the final quantitative comparison of infants with ankyloglossia experiencing GI signs.

**Results:** The search identified four research articles that showed statistically significant decreases in Infant Gastroesophageal Reflux Questionnaire Revised (I-GERQ-R) total scores in infants with ankyloglossia who had undergone surgical release via frenotomy. Vomiting and hematemesis were also found in some infants with ankyloglossia.

**Conclusions:** The most prevalent GI sign related to ankyloglossia in infants was gastroesophageal reflux. Though common in early life, it is believed that aerophagia due to ankyloglossia may be a possible etiology for reflux in this population. Clinical implication is important in investigating possible differential diagnoses associated with reflux, including ankyloglossia. Further research is needed to better understand the physiologic rationale for GI signs in infants with ankyloglossia, and how these may improve over time following treatment via frenotomy.

**Keywords:** Ankyloglossia; infant; gastrointestinal signs (GI signs); frenotomy; tongue tie

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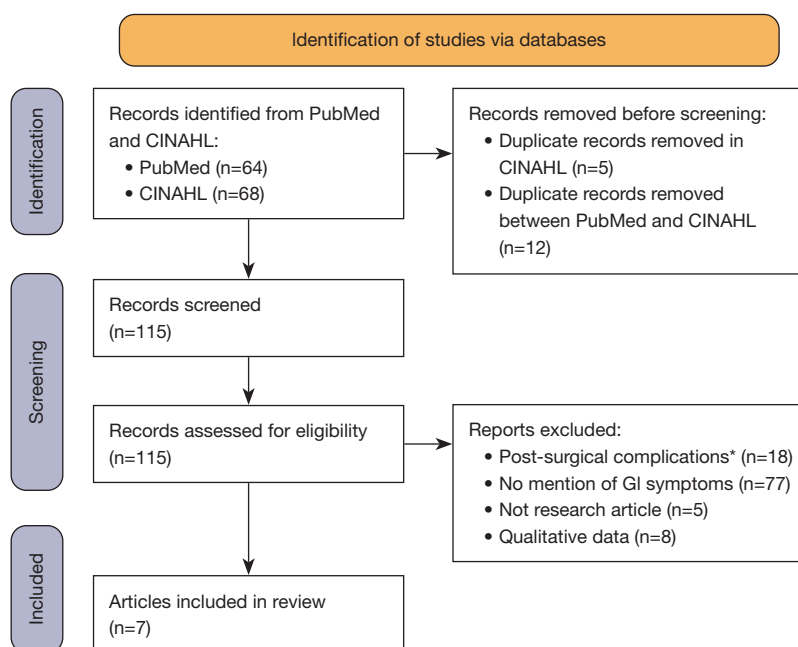
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**Figure 1** PRISMA 2020 flow diagram from Page *et al.* (19). \*, post-surgical complication articles were excluded due to mentions of anesthesia complication, bleeding complications, or other surgical complications that are irrelevant to the review. GI, gastrointestinal.

## Methods

### Search method

Using PubMed and CINAHL, an advanced search on GI signs and symptoms in infants with ankyloglossia was done using MeSH terms, relevant keywords, and filters for infant age (Figure 1). The search on PubMed, (“Ankyloglossia”[Mesh] OR “tongue tie AND (“Gastroesophageal Reflux”[Mesh] OR “Signs and Symptoms, Digestive”[Mesh] OR “gastrointestinal” OR “reflux” OR “constipation” OR “hiccups” OR “gagging” OR “flatulence” OR “aspiration” OR “latch” OR “breastfeed”) with filter applied: “Infant: birth–23 months, Infant: 1–23 months”, resulted in 64 articles. The search on CINAHL, “MH ankyloglossia or tongue tie or tongue-tie” resulted in 68 articles. After 17 duplicates were removed, a total of 115 articles were found.

### Search criteria

Inclusion criteria were: written in the English language, peer-reviewed research article, children less than 23 months of age, relevant GI signs, and quantitative data. A pre-set filter of infant per PubMed and CINAHL determined infancy age to range from birth to 23 months. In addition,

due to the limited published work regarding ankyloglossia, time parameter of the research articles was not restricted to increase access to all information on the topic. All articles from inception to the date of the search on March 31, 2023, were considered. Articles that were not original research or were qualitative in nature, research in children over two years of age, and/or articles that did not include evaluation of GI signs were excluded from this review. A total of 115 abstracts were reviewed by both authors. Articles were reviewed in full by the first author, followed by discussion between both authors to resolve discrepancies. The seven articles selected full inclusion were reviewed independently by both authors to retrieve relevant data reported in this scoping review. Both authors worked independently to retrieve data from the reports. The first author used a systematic method for retrieval data from the seven included studies. First, the author extracted the sample size, infant age range, the measurement tool(s) used to evaluate GI signs, and the time frame for assessment using the measurement tool(s). Next, the author retrieved the GI signs study investigators proposed to be associated with ankyloglossia and the study outcome(s). Finally, both authors discussed the data extraction to address and resolve any discrepancies. It was not necessary to obtain additional data from study investigators.

### *Measurement tools used in research*

A summary of each measurement tool used in the included research articles for this scoping review is provided.

#### **Infant Gastroesophageal Reflux Questionnaire Revised (I-GERQ-R)**

The I-GERQ-R is a 12-item caregiver-reported questionnaire that was derived from a 138-item I-GERQ that measures signs associated with reflux (20). The purpose of the revised version is for use in clinical trials to determine the effectiveness of an intervention on GER (20). The I-GERQ-R has a score range of 0 to 40, with a score greater or equal to 16 suggesting a diagnosis of GER, provided a thorough history and physical exam supports the diagnosis (20). One study suggested that a change in score of 6 points between time points can be considered clinically significant; however, a difference of three or four has been considered a minimally important difference (MID) (20). Using Cochrane's Q and  $I^2$  as a distribution-based method to assess a clinically significant difference or MID in the I-GERQ-R scoring, the authors determined consistency in the change of scores in multiple study designs, suggesting validity and reliability of this tool (20).

Kleinman *et al.* (21) conducted a study with 278 infant caregivers to assess the validity and reliability of the I-GERQ-R. The authors assessed a comparison and a control group, with report of daily signs and symptoms, correlation to physician-rated severity, and correlation to caregiver-rated severity (21). All comparisons were statistically significant ( $P<0.05$ ) suggesting validity of the questionnaire (21).

#### **Infant Gastrointestinal Symptoms Questionnaire (GSQ-I)**

The GSQ-I is a 13-item caregiver-reported GI-related feeding behaviors questionnaire that assesses feeding tolerance in infants, focusing on digestive and elimination patterns over the last week. Likert scales are used, with scores ranging from 1 (no symptoms) to 5 (severe symptoms). A minimum score of 13 indicates no GI distress with a score of 65 indicating extreme GI distress (22). Riley *et al.* (22) tested the validity and reliability of GSQ-I through four studies assessing interrater reliability, retest reliability, and validity. To test interrater reliability, parents were interviewed twice on the same day to evaluate their ability to repeat the same answers. They found that there was little to no change in their answers (22). To assess retest reliability, parents took the questionnaire on day 1 and

day 9. One limitation in this measure is the GI maturity in infants over time. Parents were asked to follow daily GI signs closely that could affect their answers by day 9 (22). Lastly, these same authors examined validity by comparing scores between two groups (with and without GI signs) that demonstrated statistical significance ( $P<0.0001$ ) in differences of scores supporting accurate measurement of GI signs using the GSQ-I. As this is a caregiver-report, the validity and reliability of the measured construct may be limited by parental recall (22).

## **Results**

### *GI signs associated with ankyloglossia*

Reflux, vomiting, hematemesis, and regurgitation were the associated signs found in infants with ankyloglossia (*Table 1*).

### **Reflux**

Six out of the seven included research articles mention reflux as a GI sign in infants with ankyloglossia. Ghaheri *et al.* (23) and Hill *et al.* (27) asked mothers about symptom complaints for their infants diagnosed with ankyloglossia. Hill *et al.* (27) found approximately 12 percent ( $n=13$ ) of 113 mothers had concerns about infantile reflux (seeking diagnosis). Ghaheri *et al.* (23) demonstrated that 45% of 237 ( $n=106$ ) mothers reported signs associated with reflux in their infants at the start of the study (i.e., arching of the back, unable to lay flat after eating). Neither study reported a formal diagnosis of reflux by a healthcare provider, a limitation of both studies. Ghaheri *et al.* (23,26) also measured GI signs of reflux in two studies using I-GERQ-R scores preoperatively, 1 week and 1 month after frenotomy, with a similar approach by Slagter *et al.* (24) and Hand *et al.* (25). Slagter *et al.* (24) is the first study to follow-up longitudinally at 6 months post-frenotomy demonstrating a continued downward trend of I-GERQ-R mean total scores in infants (*Figure 2*). There was a significant decrease in I-GERQ-R scores at both 1- and 6-month time points (*Table 1*). A statistically significant, all values  $P<0.05$ , decline in total I-GERQ-R scores were present in all four studies (*Figure 2*). In 2022, Ghaheri *et al.* (10) measured reflux signs such as using the GSQ-I on day 0 and day 10 post-frenotomy. The authors found a statistically significant improvement between day 0 and day 10 on GSQ-I mean scores. It is unclear if these scores correlated with clinical significance. Two of the above studies suggest aerophagia as a potential cause of reflex (12,26). Imaging or auscultation

**Table 1** Included articles' summary

Author, year	Sample (mean infant age and standard deviation)	Symptoms	Assessment	Outcome
Ghaheeri <i>et al.</i> 2017, (23)	N=237; full-term infants ages 0–12 weeks (4.4 and 3.3 weeks)	Reflux	Caregiver reported/ I-GERQ-R—preoperative, 1 week, and 1 month postoperative	At time of enrollment, 45% complained of reflux symptoms. Decrease of I-GERQ-R mean score of ~5 points between preoperative and 1 month postoperative. P value <0.001*
Ghaheeri <i>et al.</i> 2022, (10)	N=47; full-term infants ages 3–16 weeks (8.3 and 8.9 weeks): n=23; control without surgical intervention; n=24; with surgical intervention	Reflux/ vomiting/ regurgitation	GSQ-I—day 0 and day 10	Negative scores in GSQ-I scores in infants undergone surgical intervention between day 0 and day 10 while control group remained positive. All values have a P value <0.05* except for GSQ-I item for frequency of irritability/fussiness and severity of choking/gagging
Slagter <i>et al.</i> 2021, (24)	N=172; full-term infants. Lost 26 for follow-up to 6 months (N=149). Mean age and standard deviation not reported, all 3 months of age or less	Reflux	I-GERQ-R preoperative, 1 week, 1 month, and 6 months postoperative	Mean scores decreased ~8 points from pre-op to 6 months post-op. P value <0.007*
Ramoser <i>et al.</i> 2019, (11)	N=295; ages 0–52 weeks with a median age of 6 weeks	Vomiting/ hematemeses	Patients' clinical reports	23/295 experience GI symptoms. No significance level analyses done by author
Hand <i>et al.</i> 2020, (25)	N=132; infants ages 0–12 weeks (43 days)	Reflux	I-GERQ-R—preoperative, 1 week and 1 month postoperative	74% complain of reflux. Decrease of mean score by ~7 from pre-op to 1 month post-op. P value <0.05*
Ghaheeri <i>et al.</i> 2018, (26)	N=54; full-term infants ages 0–9 months (4.4 and 3.6 months)	Reflux	I-GERQ-R—preoperative, 1 week and 1 month postoperative	Decrease of mean score by ~5 from pre-op to 1 month post-op. P value <0.01*
Hill <i>et al.</i> 2021, (27)	N=113; mothers over the age of 18 with infants with tongue-tie diagnosed under 12 months (6.3 and 6.4 weeks)	Reflux	Caregiver reported	13/113 have had reflux. P value =0.05*

\*, P value is considered statistically significant  $P \leq 0.05$ ; demonstrating that there is a relationship between the two variables in the study or that the relationship between reflux and ankyloglossia correction are not by chance (28). I-GERQ-R, Infant Gastroesophageal Reflux Questionnaire Revised; GSQ-I, Infant Gastrointestinal Symptoms Questionnaire; GI, gastrointestinal.

to confirm excess air in the abdomen would help support this postulation in future research.

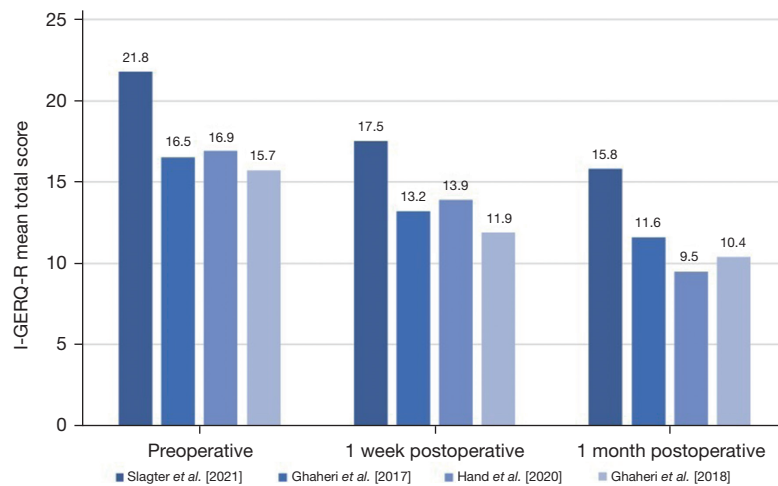
### Other GI signs

Ramoser *et al.* (11) explored the short-term (1 to 18 weeks after frenotomy) and long-term (15 months after frenotomy) outcomes of signs associated with ankyloglossia in 295 infants. Twenty-three infants (8% of the total sample) experienced signs of aerophagia, vomiting, and hematemeses. The short-term outcomes after frenotomy showed improvement signs in 84% of infants (n=247). Specifically, there were improvements in latch onto the

breast, decreased nipple pain, less aerophagia, reduction in episodes of vomiting, and resolution of hematemeses. Long term outcomes demonstrated continued improvement in these signs for 77% of participants (n=227) (11).

### Quality analysis on included articles

The research articles included in this review were rated based on the John Hopkins Evidenced-Based Quality Scale (29,30). This scale rates both evidence and quality of research, with level 1 representing the highest evidence (e.g., randomized control trial) and A quality providing



**Figure 2** Visualization of the I-GERQ-R total mean scores differences between preoperative and postoperative treatment in four different research articles. Slagter *et al.* [2021] (24) has a quantitative reported value of 13.6 (mean) and 3.9 (standard deviation) at 6-month postoperative showing further improvement in I-GERQ-R total mean scores. P value for all values <0.05. P value is considered statistically significant when  $P \leq 0.05$ ; demonstrating that there is a relationship between the two variables in the study or that the relationship between reflux and ankyloglossia correction are not by chance (28). I-GERQ-R, Infant Gastroesophageal Reflux Questionnaire Revised.

generalizable and consistent results (29). Research articles by Ghaheri *et al.* (23,26), Slagter *et al.* (24), Ramoser *et al.* (11), and Hand *et al.* (25) were considered Level II of good quality, B, due to their quasi-experimental design, sufficient sample size, consistency, and definitive conclusions. The quasi-experimental design is non-randomized, evaluating an intervention, to demonstrate its relationship with an outcome. In these studies, frenotomy to treat ankyloglossia was the intervention of interest. The relationship between frenotomy and improvement in GI signs using the previously described screening tools was the desired outcome in these studies (31). These studies did not include a control group due to ethical considerations (16,32). The ethical considerations need to benefit the parties involved in human studies (32). By having a control group, these studies could raise ethical issues in the lack of intervention for those showing signs that may be due to ankyloglossia, and the potential effects on feeding that could impair growth and development. In all studies included, it was unclear what other interventions may have been used concurrently alongside frenotomy, such as lactation support or thickened feedings. It is also critical to recognize the maturity of the GI tract that occurs over time that may have resulted in improved reflux signs. Lastly, there are several different classification systems to diagnose ankyloglossia, none of which have been thoroughly tested for validity

and reliability, limiting our ability to compare severity of ankyloglossia between studies and the relationship between severity and signs of reflux.

Ghaheri *et al.* (10) was assessed as Level II and lower quality, C, due to its limited sample size and lower quality conclusions. The research article was able to quantitatively identify a relationship between reflux and ankyloglossia with statistically significant differences between day 0 and day 10 GSQ-I scores on those with surgical treatment compared to an observational group (10). However, the similarities in the answers and scores on the GSQ-I of day 0 between the observational group and surgical treatment group were not statistically significant (10). This does not mean that there is a lack of similarities in the comparisons but that it did not meet the standard cut off to achieve statistical significance (33). Lastly, the research by Hill *et al.* (27) is classified as Level V, with B-level quality, due to lack of experimentation. The authors were able to draw fair conclusions with clear aims and objectives in evaluating the relationship between ankyloglossia and GI signs (9,27).

## Discussion

### *Key findings and strengths*

This scoping review critiqued seven articles on GI signs

in infants with ankyloglossia. As defined, ankyloglossia is the restriction of tongue mobility and stability due to anatomical differences in the lingual frenulum (2,3). Six out of the seven articles discussed the presence of GER in infants with ankyloglossia, with improvement post-frenotomy in both short and long-term follow-up. GER is a common sign amongst infants under the age of 6 months, considered to be a normal GI variation early in life (13,20). The etiology of reflux is unclear, but presumed mechanisms include transient lower esophageal sphincter relaxations unassociated with swallowing, delayed gastric emptying, and other respiratory tract mechanisms (13). However, within review, there were both statistically and clinically significant improvements in reflux following treatment of ankyloglossia via frenotomy. This may suggest that reflux in infants with ankyloglossia may extend beyond the normal spectrum of signs expected early in life.

This review encourages us to consider ankyloglossia as a possible etiology for reflux, given its improvement after treatment of the oral restriction. Maternal concerns of reflux for infants with ankyloglossia signs were discussed in two studies (23,27). Four of the articles demonstrated mean I-GERQ-R scores that indicated “severe” reflux in infants with untreated ankyloglossia (*Figure 2*), with decreased in scores post-surgical intervention. Improving tongue mobility with frenotomy may positively impact both latch and swallowing. While most studies are limited to short-term follow-up, signs of reflux were reduced at 1-week, 1-month, and 6-month post-frenotomy (*Figure 2*). The difference in the mean total I-GERQ-R scores preoperative to postoperative ranged from 5 to 8 (*Figure 2*), with differences in scores above 6 considered statistically significant (20). Aerophagia was also one of the caregiver-reported signs present in infants with ankyloglossia (11), though this cannot be confirmed without physical examination or radiographic studies.

Other findings were Ghaheri *et al.* (10) used the GSQ-I to score specific symptoms that can lead to reflux and Ramoser *et al.* (11) detailed caregiver reported signs of vomiting and hematemesis. It is important to note, however, that hematemesis can be caused by other underlying issues beyond ankyloglossia such as esophagitis from GERD, ulcers, or swallowed maternal blood (34). A case study by Brooks *et al.* (9) showed aspiration and significant dysphagia during feeding for one infant with ankyloglossia. This was postulated to cause reflux and needs to be evaluated in future research with a larger sample.

### *Limitations*

Beyond those discussed throughout this scoping review, additional limitations include the limited research on this subject, differing study methods (i.e., sample size, questionnaires, follow-up), the highly disputed definition of ankyloglossia, and the presumptive association between ankyloglossia and reported GI signs without other differential diagnoses discussed or considered. While the overall quality of the included research was fair, more research is necessary. Future research could be strengthened by the inclusion of control groups, larger sample sizes, use of one consistent definition and classification of ankyloglossia, and longitudinal data on GI signs.

### *Clinical implications and future research*

GER is commonly mis- and over-diagnosed without proper treatment or consideration for other diagnoses (12). GER represents the backward movement of gastric contents into the esophagus while GERD affects daily life and contributes to complications such as erosion of the esophagus, often requiring pharmacologic treatment. The recommended treatments for GER are thickened liquids, hydrolyzed protein-based formula, or eventually, invasive pharmacological treatment (13,34). Recent research has demonstrated negative sequelae of pharmacologic treatment options (35), with providers opting for non-pharmacologic management (e.g., thickened liquids, remaining upright after feeding). Many factors can affect the conservative treatment of thickeners such as nutritional properties, precipitation from thickeners, and bowel morbidities (36). By recognizing the long-term implications of conservative and invasive treatments that may cause side and adverse effects (2,12), it is important to first investigate possible differential diagnoses associated with reflux, including ankyloglossia. To screen for ankyloglossia, the healthcare provider should use screening tools such as the Hazelbaker Assessment Tool for Lingual Frenulum Function, the Coryllos system, and/or The Martinelli Lingual Frenulum Protocol and evaluate appearance, function, and impact on feeding (2). It is important to note that the appearance of the tongue alone does not provide sufficient data to support frenotomy.

Further research is necessary to quantify the relationship between ankyloglossia and reflux; this scoping review serves as an important summary for clinicians to assess for ankyloglossia and consider specialty referral and

possible surgical intervention as one way to improve reflux. However, it is important to recognize that in all seven studies included in this scoping review, mean infant age was less than 6 months. With reflux considered a normal occurrence in this age group, more research is necessary to evaluate longitudinal improvement in reflux for infants with ankyloglossia without surgical intervention. Maternal breastfeeding symptoms, parental distress, and quality of life should also be considered when making the decision to treat.

Beyond reflux, other pharyngeal and GI signs such as vomiting, hematemesis, and regurgitation should be explored in future research. Although frenotomy is deemed a minor surgical intervention, there have been rare complications reported including bleeding, infection, scarring, and need for additional intervention (2,12). It is unclear which children benefit most from the procedure and who should undergo treatment. Future research is needed to explore GI signs to determine when surgical intervention is necessary to relieve reflux and reduce the use of potentially harmful treatments.

## Conclusions

This scoping review has summarized GI signs in infants with ankyloglossia, comparing these before and after treatment via frenotomy. Most notably, signs of reflux improved with ankyloglossia treatment, suggesting a relationship between GI signs and ankyloglossia. Future research is required to further investigate the association between GI signs/symptoms and ankyloglossia; as well as the physiologic rationale for these findings.

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