Mothers' experiences of breastfeeding a child with tongue-tie

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Abstract
Tongue-tie is characterized by an abnormally tight, short and thick lingual frenulum restricting the tongue's movement. This functional impairment can hinder a child's ability to maintain an effective latch and suckle and may lead to complex breastfeeding difficulties. The primary aim of this study was to explore the experiences of mothers who have breastfed a child with tongue-tie, including their experiences with the health care system. A qualitative description study design was used. Two semistructured focus groups were conducted in February 2016 with a total of nine participants in the largest metropolitan area of Newfoundland and Labrador, Canada. Content analysis using constant comparison revealed a common incongruity between participants' breastfeeding expectations and their actual experiences of feeding a child with tongue-tie. Three major themes are discussed: mothers' well-being, strained interpersonal relationships and frustration with the health care system.

KEYWORDS
breastfeeding, focus group, infant feeding, qualitative description, tongue-tie

1 | INTRODUCTION

The benefits of breastfeeding to mother and baby are well established; however, rates of initiation and duration remain lower than recommended in many parts of the world (World Health Organization, 2019). In response to very low rates of breastfeeding, the Canadian province of Newfoundland and Labrador (NL) established the Baby-Friendly Council in 2009. As a first step, the Council identified a need for empirical research to inform evidence-based programmes and policies to protect, promote and support breastfeeding. Over the last decade, breastfeeding initiation improved significantly from 64% in 2007 to 76% in 2017; however, exclusivity to 6 months remains very low at 15% (Perinatal Program Newfoundland and Labrador, 2017). These data raise an important question: for many mothers who intend to breastfeed, what factors complicate the breastfeeding experience and lead to early breastfeeding cessation? This question has become a major focus of the Baby-Friendly Council of NL, as members of our research team seek to understand infant feeding practices through analysis of survey data collected in our province-wide cohort study Feeding infants in Newfoundland and Labrador (FiNaL) (Alkusayer et al., 2018; Temple Newhook et al., 2017; Twells et al., 2016) and through a number of qualitative research studies (Ludlow et al., 2012; Temple Newhook et al., 2013; Young et al., 2016).

Consistent with other research (Geddes, Chadwick, Kent, Garbin, & Hartmann, 2010; Riskin et al., 2014; Segal, Stephenson, Dawes, & Feldman, 2007), preliminary analysis of data from the FiNaL study indicate that for mothers who intend to breastfeed, tongue-tie, an abnormally tight, short and thick lingual frenulum, may complicate the breastfeeding experience. The functional impairment can hinder a...
child’s ability to maintain an effective latch and suckle (Hong et al., 2010; Miranda & Milroy, 2010). In addition to difficulties with the mechanics of feeding, tongue-tie can have a negative psychosocial impact on the breastfeeding relationship and maternal mental health (Edmunds, Fulbrook, & Miles, 2013; Wong, Patel, Cohen, & Levi, 2017) and may lead to early cessation of breastfeeding (Edmunds, Fulbrook, & Miles, 2013; Muldoon, Gallagher, McGuinness, & Smith, 2017). Where tongue-tie leads to major breastfeeding difficulties, a frenotomy, more commonly referred to as a ‘release’, a simple incision of a tongue-tie with surgical scissors, laser or a scalpel, may be deemed necessary (Rowan-Legg, 2015).

The prevalence of tongue-tie ranges between 0.02% and 10.7% of newborns (Power & Murphy, 2015). The prevalence of tongue-tie in NL is unknown; however, awareness of the condition is increasing, especially among mothers who experience challenges with breastfeeding. According to the data from the FiNaL study, mothers who experienced breastfeeding challenges due to tongue-tie reported a high level of frustration with access to assessment, diagnosis and management. Based on these findings and the increasing number of issues cited by mothers on local social media support groups, the current research was deemed necessary. Our study aimed to explore the experiences of mothers who have breastfed a child with tongue-tie and their experiences with the health care system.

2 | METHODS

2.1 | Study design and sample

Consistent with the aim of qualitative description proposed by Sandelowski (2000, 2010), we sought to provide a descriptive account of mothers’ experiences and the resultant meaning they ascribed to their experiences. Purposive sampling was used to select participants who could contribute detailed information to enhance our understanding of the experiences of mothers who had breastfed a child with tongue-tie. Participants were recruited using an advertisement that was shared with two local social media groups. Eligibility for the study required that participants were at least 19 years of age, had breastfed a child with tongue-tie in the last 3 years for any duration and were available for one of two focus groups. Mothers were invited to bring their children to the session. A total of 16 participants were recruited to participate; five participants were scheduled to take part in the first focus group and 11 in the second. However, only three and six attended respectively. Participants who were unable to attend cited family illness and difficulties with child care. The sociodemographics of the sample are presented in Table 1.

2.2 | Data collection

Two focus groups were held in St. John’s, NL, Canada, in February of 2016. We chose to use focus groups as our method of data collection, as it was felt that the group interaction, dynamics and conversation would provide a rich and deep account of mothers’ experiences with little interference from the researcher (Green & Thorogood, 2018). In addition, focus groups would create a supportive environment for mothers to connect with peers and discuss their experiences.

The focus groups were led by the first author, a graduate student, under the guidance and supervision of a qualitative investigator with experience in focus group research. A third researcher also attended the sessions. Consent was obtained, and the conduct and guidance of the focus groups were explained. A self-administered questionnaire was distributed prior to commencing the focus group to capture participant characteristics. A semistructured and open-ended discussion guide was used. A sample of the interview questions is provided in Table 2. Each focus group lasted between 60 and 90 min and was audio-recorded. All three researchers engaged in note taking throughout the sessions and debriefed following the completion of each focus group. The first author recorded her reflections on the conversations. Researcher field notes helped identify questions that elicited the greatest emotional response, agreement or discordance among participants and group dynamics.

2.3 | Data analysis

The audio-recordings were transcribed verbatim and checked for quality and accuracy. No identifying details were attached to the transcripts, as participants were assigned a numeric code. Data were analysed using the conventional approach to content analysis, which ensures data-driven coding and categorization using the participants’ own words instead of preconceived, researcher imposed, categories (Hsieh & Shannon, 2005). This method of analysis was chosen because it stays close to the data, aligning with qualitative description and the aim of our study, which was to describe a phenomenon where
Two researchers who attended the focus groups engaged in independent and manual coding. The research team met to discuss the codes, resolve discrepancies and generate an initial coding template. Transcripts were re-coded by the same two researchers and themes identified by the continuous comparison of coded items within and between the groups of participants (Merriam, 2009). After the second focus group, data saturation was reached, as no new information had emerged and no new codes were identified (Bradshaw, Atkinson, & Doody, 2017). All members of the research team were involved in refining the themes and resolving discrepancies through discussion and consensus. To strengthen the trustworthiness of the findings, participants’ own words were used as exemplars throughout the analysis (Bradshaw, Atkinson, & Doody, 2017; Colorafi & Evans, 2016).

### 2.4  Ethical considerations

Ethics approval for this study was obtained from the Newfoundland and Labrador Health Research Ethics Board, Reference No. 15.248.

### 3  RESULTS

All nine participants in our study had intended to breastfeed prenatally. Five of the nine had breastfed more than one child, and three had breastfed more than one child with tongue-tie. Only one participant reported that her child’s tongue-tie was diagnosed by a paediatrician prior to hospital discharge. The remaining participants noted that their child’s tongue-tie was diagnosed in the community by a public health nurse, family physician, dentist, lactation consultant, doula or by self-diagnosis. The age of diagnosis varied from 1 to 2 years old, with just under 60% (i.e. seven of 12 infants represented by our nine participants) diagnosed in the first 2 weeks of life. All elected to have their child’s tongue-tie released.

In both focus groups, participants described their experiences and perspectives on feeding a child with tongue-tie, bringing forth a common incongruity between their prenatal expectations of breastfeeding and actual experiences. We discuss three major themes here: mothers’ well-being, strained interpersonal relationships and frustration with the health care system.

#### 3.1  Mothers’ well-being

The majority of stories shared by participants were touched by similar experiences and emotion, with three main factors (subthemes) influencing their well-being: physical pain; desperation, guilt and disappointment; and resilience.

#### 3.1.1  Physical pain

Almost all the participants verbalized the incredible amount of pain they endured when breastfeeding a child with tongue-tie. The words of one participant in the first focus group exemplify this pain.

> I didn’t want to latch my baby to my breast because I knew it would be excruciatingly painful. Toe-curling, foot stamping [...]. I tried all the different positions, and all the different pillows, and all the different chairs, and all the different everything... the latch was good but it was so painful. (Focus Group [FG] 1; P3)

Many participants also talked about the physical damage to their bodies. A participant in the second focus group spoke candidly about the trauma to her nipples:

> I didn’t want to latch my baby to my breast because I knew it would be excruciatingly painful. Toe-curling, foot stamping [...]. I tried all the different positions, and all the different pillows, and all the different chairs, and all the different everything... the latch was good but it was so painful. (Focus Group [FG] 1; P3)
I had a lot of pain, and like really ... I called them like gouges; huge gouge sores on my nipples that were like down to the tissue. Every time [baby] would latch on, tears would stream down my face. It was very painful. (FG 2; P6)

As the participants shared their experiences with pain while trying to breastfeed, it was evident that this physical pain negatively affected their emotional well-being.

### 3.1.2 | Feelings of desperation, guilt and disappointment

Most participants described an overwhelming desperation to figure out what was going on with their child. They felt isolated by their experiences and unsure of where to turn for help.

I don't think I can stress enough how desperate I was when things, like really got bad [...]. My nipples were like beyond painful, I was like holding her hand every time she latched on so that I could like, not grab and scream at something ... You have to feed your baby, so you do become desperate for any support. (FG 2; P6)

[The baby] was slipping off, he wasn't interested in latching ... we were trying [to breastfeed] around the clock, and I knew what I was doing [given prior breastfeeding experience] [...]. So, I trenched out into a snowstorm because I felt like it was really important to have him weighed ... I was worried that he wasn't latching on. (FG 2; P2)

As the participants told their stories, one thing was very clear: They were all just trying to do what was best for their child. Many reported feeling guilt for what their child had endured, blaming themselves for not being able to 'breastfeed properly', and for feeling dread each time their child latched onto the breast.

I have a lot of regret for not knowing that he was tied and the pain that he went through ... for months ... and learning to eat and you know, everybody just telling me, 'He just needs to cry it out' [...]. All the regret I have for listening to other people, and telling me that it's normal, babies cry ... it's not normal, it's not. (FG 2; P3)

Every time she would latch it was so painful, I dreaded having to feed her, and then you're feeling guilty because you're dreading feeding your baby, but you need to feed your baby ... it was awful. (FG 2; P6)

Many of the participants felt let down by their breastfeeding experience and had a distinct sense of disappointment. Some participants, especially first-time mothers, spoke to the fact that they did not anticipate breastfeeding to be so difficult. This is exemplified by the words of one participant who never achieved the breastfeeding relationship she hoped to have with her child and used a supplemental nursing system for months in order to breastfeed.

How much time did I spend trying to force this breastfeeding relationship to work when ... for what? You know, when I spent half my maternity leave literally at a doctor's appointment, or physio, or craniosacral, or breastfeeding clinic, probably almost every day for months. (FG 2; P5)

The sense of disappointment was not unique to first-time mothers. For example, a multiparous participant who previously breastfed recalled:

It hurt, and it felt like matches on my nipples. I just remember thinking there's something wrong with [the baby], like she should be able to eat, she couldn't get a latch. I didn't have the same light feeling ... when the oxytocin just kinda pumps through you as you're breastfeeding ... I didn't get that feeling with her. (FG 2; P3)

### 3.1.3 | Resilience

Despite these challenges, participants also demonstrated resilience, as evidenced by their determination for self-advocacy and to sustain their breastfeeding relationship. This often led participants to educate themselves and use their knowledge to advocate for their own children and for other families.

I've found that like ... you have to advocate for yourself, you have to become an expert, a mini expert in all these things. (FG 1; P2)

Resilience was illustrated by the mothers' determination to breastfeed no matter the obstacles they had to overcome.

We're still breastfeeding now, because at this point, I said, 'I'm doing this, I don't care what has to happen.' (FG 1; P1)

I went through a year of blocked ducts. [Speaking to baby in her arms] You are nursing until you are a teenager. (FG 2; P3)

In closing out the second focus group, a participant acknowledged the resilience of her peers:

I just want to applaud everybody here for just being so resilient and keeping trying, because it's so easy to say
I can’t do this anymore! You know ... you have those feelings even when you have a baby who doesn’t have any trouble breastfeeding, and then when you have a baby who is struggling, and you’re worried ... it’s hard. (FG 2; P2)

3.2 | Strained interpersonal relationships

Participants described how their experience of breastfeeding a child with tongue-tie affected the many relationships in their lives, including the relationship with their partner, children, other family members and friends. Two participants who had breastfed more than one child with tongue-tie explained:

I think it wrecked my marriage ... we struggle as parents, we struggle together. (FG 2; P3)

I think it definitely put strain ... between [my husband] and me. (FG 1; P2)

Some participants’ family or friends did not agree with the choices they made regarding their child’s tongue-tie, sometimes simply not believing that it was an actual ‘thing’.

My parents didn’t understand why [the frenotomy] was necessary ... I think it ... because they think it has some voodoo [...]. If someone doesn’t understand the wealth of information that the parents amass before they decide to get this surgery for their kid, it can put a strain on that relationship. (FG 2; P4)

On a broader scale, participants felt that societal perception of breastfeeding made it even more difficult to navigate different views of family and friends, leaving mothers to defend their desire to salvage their breastfeeding relationship.

I felt like I was constantly on the defense, like defending my decision to keep going, even though we were having so much trouble. (FG 1; P1)

Those who were multiparous described their strained relationships with other children at home. Many struggled to take care of their other children, as the child with tongue-tie seemed to dominate so much of their time and patience.

I think what I found tough was that I wasn’t giving to my older child the attention that he needed, and he was really struggling with the fact that Mommy is breastfeeding another baby ... But, I had to focus on [my younger son], he needed me, he struggled, he fed around the clock. (FG 2; P2)

3.3 | Frustration with the health care system

Participants expressed considerable frustration with the health care they received. This theme dominated both focus group discussions. A few participants were brought to tears when describing their experiences with the health care system. The main factors that contributed to their frustration were dismissal, lack of priority for the breastfeeding relationship and distrust. In this context, participants provided a number of recommendations to improve the care of breastfeeding dyads challenged by tongue-tie.

3.3.1 | Dismissal

The experience of feeling dismissed by health care providers was commonly expressed, whether participants were looking for answers to the feeding challenges they faced, poor infant weight gain or tongue-tie management. They perceived that their voices were not often heard. This had a profound effect on their emotional well-being and perpetuated feelings of frustration with the health care system. A participant’s quote expresses this clearly:

I was really upset, really, really upset ... I was like, how many times do I need to ask for help and be told, ‘you’re fine!’ And then [explain], ‘I’m not making it up, I’m not crazy, this is actually something happening ... my baby’s symptoms are real and my symptoms are real, and ... it really hurts! This isn’t normal!’ (FG 1; P3)

An exchange between two participants in the first focus group also exemplifies this finding:

Participant 1: I went to public health and the breastfeeding clinic and everything after I had it revised. Up until that point, nobody really took me seriously, ... or, even, my mental health or anything. Like I just felt like ... it was so emotionally damaging to me.

Participant 3: [interrupts] And exhausting.

Participant 1: You know, you’re obsessed with this ... and not a whole lot of people understand it and [...] I didn’t have anyone.

Participant 3: Yeah, you just feel alone, you feel like nobody understands, especially when everyone was saying ‘the latch is fine!’
3.3.2 | Lack of priority for the breastfeeding relationship

Even though the majority of participants had been counselled that ‘breast is best’, when they had breastfeeding issues, they were often encouraged by health care providers to ‘go to the bottle’. This discrepancy created a perception among the mothers that there is a lack of priority for the breastfeeding relationship, which in turn further perpetuated feelings of frustration with the health care system. A conversation among participants in the first focus group illustrates this point.

Participant 2: The doctor was like, 'Well, if you're still having problems, there's always the bottle.'
Participant 3: [eye rolling] ... formula, yeah!
Participant 2: [expressing sarcasm] 'Just give him a bottle!
Participant 3: [expressing sarcasm] 'Just give him a bottle.'
Participant 2: Yeah, I was like 'that's how I came to see you.'
Participant 3: Exactly ...

The perceived lack of support for breastfeeding was echoed in participants’ perceptions of the lack of systemic support for mother-infant dyads living with tongue-tie.

I think that ... the healthcare system ... You know, there's a tragedy that happened with all of us [...] some breastfeeding experiences were taken from us and extra stress put on us [unnecessarily]. (PG 2; P2)

3.3.3 | Distrust

Participants described how their interactions with medical professionals resulted in a sense of distrust, as there was inconsistent information relayed by their providers. In many cases, they felt that they knew more about tongue-tie than the providers who cared for them. Many explained how their provider’s lack of knowledge and understanding of tongue-tie, its pathology and effect on breastfeeding caused them to question provider credibility. This was further exacerbated by interactions with providers who disregarded tongue-tie as a factor complicating the breastfeeding experience. This included family doctors; some of whom did not believe the child had a tongue-tie and refused to refer for further assessment. As a result, participants began to distrust other health care providers and questioned health care accountability, exacerbating the frustration they already felt.

There’s a little bit of a disconnect between public health and the dentist and the family doctor in terms of what information or what symptoms they thought were most important. I did have a good experience with public health though, I must say. (FG 1; P1)

3.3.4 | Recommendations for health care providers

In order to address these inconsistencies in care for breastfeeding dyads, participants had many suggestions to assist families dealing with tongue-tie. Many participants called on the health care system and providers to establish clear processes for referral, assessment and management of tongue-tie. Furthermore, they highlighted the need for additional training for health care providers as professional development or as part of the continuing medical education curriculum.

I think there has to be some sort of consistency among the healthcare professionals as to the seriousness of the tongue-tie. (FG 1; P1)

The system needs to push for somebody to be trained, and you know, followed to actually get consistent diagnosis and consistent treatment for babies who are considered to be tied. (FG 1; P2)

[Initiate] a 24/hour support line, kind of like mental health crisis line but for people with breastfeeding difficulties [...]. That would be so helpful just to know they could talk you through some things or give you some resources. (FG 2; P6)

4 | DISCUSSION

The experience of breastfeeding a child with tongue-tie varied among participants, but all agreed that it had a significant impact on their physical and emotional well-being. The experience placed strain on relationships, generated feelings of distrust and frustration with health care providers and the health care system and challenged their expectations of breastfeeding.

The impact of breastfeeding a child with tongue-tie on mothers’ physical and emotional well-being is perhaps one of the most important findings of this research. Participants’ indication that pain was one of the most significant impacts tongue-tie has on the breastfeeding experience is reflected in the literature. An infant’s restricted tongue movements may lead to painful, bleeding nipples and breast pain for the mother (Amir, Dennerstein, Garland, & Fisher, 1996; Griffiths, 2004). Researchers have shown that for every day of maternal pain during the initial 3 weeks of breastfeeding, there is a 10% to 26% risk of breastfeeding cessation (Schwartz
et al., 2002). Beyond physical trauma, participants experienced emotional pain and distress as they searched for answers and support, leading to frustration with the health care system. Similar findings were reported in two qualitative studies (Edmunds, Fulbrook, & Miles, 2013; Wong, Patel, Cohen, & Levi, 2017). Pain led to guilt for not being able to establish the breastfeeding relationship they hoped for, which ultimately led to feelings of failure along with high levels of emotional distress. Despite these negative feelings, resilience and self-advocacy prevailed as participants became informed, amassing information and sharing it with their peers, which has been shown to help individuals in coming to terms with their own experiences (Mohracher & Knorr, 2012).

The experience of feeding a child with tongue-tie can impact relationships in the mother’s life. Strained relationships with the partner were more commonly reported by multiparous participants in our study. This is an important finding because partner support has been shown to be a key factor in sustaining breastfeeding (Temple Newhook et al., 2013). Other relationships were also strained, including those with other children, family and friends. This impact on relationships can be detrimental to the breastfeeding relationship, as the attitudes and expectations of family members can strongly influence a woman’s breastfeeding experience and success (MacKean & Spragins, 2012; Temple Newhook et al., 2017).

Participants’ experiences with the health care system not only affected their emotional well-being but also opened their eyes to the lack of systemic support for families living with tongue-tie. This is not specific to those breastfeeding a child with tongue-tie, as health care culture has been described as a barrier to all breastfeeding relationships (MacKean & Spragins, 2012). As MacKean and Spragins (2012) pointed out, an unintentional consequence of describing breastfeeding as ‘natural’ is that breastfeeding challenges (e.g. cracked and painful nipples, mastitis and poor latch) and the sense of vulnerability felt by some mothers are often not talked about or acknowledged. The same can be said for the challenges that may present as a result of breastfeeding a child with tongue-tie. We agree with MacKean and Spragins (2012) that it is important for providers to openly acknowledge that the breastfeeding experience is different for everyone, with potential challenges and setbacks, therefore providing an approach that may help achieve realistic rather than overly idealistic expectations of the breastfeeding experience.

Lack of support from health care professionals can decrease a woman’s confidence in breastfeeding and result in the early cessation of breastfeeding (Doonan et al., 2018; MacKean & Spragins, 2012). In the current study, this may have been exacerbated by participants’ extra needs for health system support. It should be noted that in NL, access to breastfeeding support and assessment and care for infants who present with tongue-tie is variable. The greatest support is found in urban centres where there is access to weekly breastfeeding support groups led by public health nurses and lactation consultants, as well as the La Leche League peer support group. However, it was not until recently (i.e. after the completion of this study) that families could access the services of private lactation consultants, midwives and doulas, albeit at a cost, not covered by public health insurance. At the time this study took place, there were few providers in our province who performed frenotomies.

The participants in this study described significant inconsistencies in health care provider knowledge and acceptance of tongue-tie and its potential effects on breastfeeding. This finding is not surprising given other research documenting the considerable controversy that exists among health care providers on the clinical relevance, treatment and diagnosis of tongue-tie (Jin et al., 2018; Messner & Lalakea, 2000). It was clear that this contributed to a common feeling of distrust of health care professionals and the health care system. However, when participants encountered a provider who was willing to listen and to provide support, trusting relationships developed.

4.1 | Strengths and limitations

This study adds important information to the limited body of qualitative research describing the experiences of mothers who breastfed a child with tongue-tie. To our knowledge, there are only two qualitative studies published that have explored this topic (Edmunds, Fulbrook, & Miles, 2013; Wong, Patel, Cohen, & Levi, 2017). Although our findings are consistent with these earlier publications, our study provides an additional rich description of the taxing emotional journey experienced by mothers while also providing recommendations to health care providers and policy-makers on supports needed for breastfeeding dyads who experience feeding challenges as a result of tongue-tie.

This study has some limitations. The findings are based on a relatively small homogenous sample from one urban location within the Canadian province of Newfoundland and Labrador. It comprised participants who were all partnered, educated and financially well off. The results are therefore limited in transferability and may not be fully representative of the larger population of mothers in our province who have experience breastfeeding a child with tongue-tie. We also acknowledge the potential for a selection bias, because our study included a self-selected sample of mothers who all had difficulty breastfeeding a child with tongue-tie. Finally, respondent validation, or member checking, which involves going back to participants to review the findings (Birt, Scott, Cavers, Campbell, & Walter, 2016), was not conducted.

5 | CONCLUSION

The mothers who participated in our study reported that breastfeeding a child with tongue-tie had a significant impact on their well-being, negatively affecting both physical and emotional health. Many participants experienced excruciating physical pain and discomfort when breastfeeding; and feelings of guilt and dismissal by health care professionals were experienced. Yet there was evidence of resilience and self-advocacy. Expectations of breastfeeding were challenged and made participants question the information provided by
health care professionals. There was a lack of systemic support for families affected by tongue-tie, which in turn caused participants to distrust health care professionals’ knowledge. Future research is needed to explore the experiences of mothers across diverse populations.

These research findings have implications for practice. They will inform the health care community about the challenges some mothers experience when breastfeeding a child with tongue-tie. The findings will aid in the identification of appropriate supports for mothers of children with tongue-tie. They highlight the need for a coordinated, evidence-based approach to screening, assessment, diagnosis and management of tongue-tie. For example, robust policies regarding newborn screening for tongue-tie and community referral processes for assessment and management are needed. Furthermore, the findings will help inform the development of educational programming, clinical practice guidelines and hospital and community policies for health care professionals. We recommend health care professionals adopt a more patient-centred and individualized approach to caring for breastfeeding families.

ACKNOWLEDGMENTS

Thank you to Julie Temple (Research Associate, Janeway Pediatric Research Unit, St. John’s, NL) for providing support with data coding and analysis and to Kristin Harris Walsh (Faculty of Medicine, Memorial University, St. John’s, NL) for providing support with preparation of the manuscript. No funding was received for this project.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

CONTRIBUTIONS

This research was completed as part of JW’s master’s thesis. JW conducted the fieldwork, coding and analysis under the supervision of TL and LT. All authors were involved in regular discussions about analysis and interpretation of data and contributed to the final manuscript.

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How to cite this article: Waterman J, Lee T, Etchegary H, Drover A, Twells L. Mothers’ experiences of breastfeeding a child with tongue-tie. Matern Child Nutr. 2021;17:e13115. https://doi.org/10.1111/mcn.13115