POLIANA VALDELICE DA CRUZ

A RELAÇÃO DA PREMATURIDADE E BAIXO PESO AO NASCER COM LESÕES DE MUCOSA ORAL EM RECÉM-NASCIDOS E PREVALÊNCIA DE ANQUILOGLOSSIA DE ACORDO COM CRITÉRIOS DIAGNÓSTICOS

Faculdade de Odontologia
Universidade Federal de Minas Gerais
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Orientadora: Profª. Drª. Carolina Castro Martins
Coorientadora: Profª. Drª. Cristiane Baccin Bendo

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FOLHA DE APROVAÇÃO

Relação da prematuridade e peso ao nascer com lesões de mucosa oral em bebês, e prevalência de anquiloglossia de acordo com critérios diagnósticos

POLIANA VALDELICE DA CRUZ

Tese submetida à Banca Examinadora designada pelo Colegiado do Programa de Pós-Graduação em Odontologia, como requisito para obtenção do grau de Doutor, área de concentração Odontopediatria.
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“Despeça-se de suas fases. Não se apegue ao que foi bom, nem tampouco crie vínculos com os acontecimentos que lhe causaram dor. É no movimento de passagem que criamos espaço para o novo que há de chegar. Reinaugure-se diariamente. Conceda-se a graça de um outro renascimento. A vida nunca se opõe aos que se dispõem às regras do plantio diário.”

Pe. Fábio de Melo

RESUMO

Objetivo: 1) verificar a associação da prematuridade e baixo peso ao nascimento (BPN) com a ocorrência de lesões de mucosa oral em recém-nascidos (RN), fatores de saúde materno-infantil e socioeconômicos, por meio de um estudo transversal; e 2) avaliar a prevalência de anquiloglossia em bebês, crianças e adolescentes de acordo com diferentes critérios diagnósticos, por meio de uma revisão sistemática. **Métodos:** 1) O estudo contou com uma amostra de 431 pares de mães e recém-nascidos. A coleta foi realizada no período de agosto de 2016 a abril de 2017. Após o nascimento, os bebês tiveram a cavidade bucal examinada para lesões de mucosa. A regressão logística bivariada e multivariada foi utilizada para a análise dos dados. O nível de significância foi de 5%. 2) Foram realizadas buscas eletrônicas em nove bases de dados até 2021. Por meio da meta-análise de efeitos aleatórios, foi avaliada a prevalência bruta de anquiloglossia e para sexo. Uma meta-análise de efeitos mistos foi usada para análise de sugrupos por critérios diagnósticos e idade. Calculamos a RP e o IC de 95% da ocorrência de anquiloglossia em meninos, em comparação com meninas e avaliamos a certeza das evidências usando a abordagem GRADE. **Resultados:** 1) Prematuridade e BPN foram associados com pérolas de Epstein (odds ratio [OR]: 1,7; intervalo de confiança de 95% [IC]: 1,03–3,0; OR: 1,8; IC95%: 1,1–3,2, respectivamente) e mucocele (OR: 4,6; IC95%: 1,3–16,1; OR: 3,7; IC95%: 1,1–13,1, respectivamente), mas não à anquiloglossia (OR: 1,0; IC95%: 0,5–2,1; OR: 0,7; IC95%: 0,3 -1,6, respectivamente) ou amamentação (OR: 0,5; IC95%: 0,1-2,1; OR: 1,9; IC95%: 0,2-15,6, respectivamente). A prematuridade foi associada à gravidez de alto risco (OR: 2,3; IC 95%: 1,3–3,9), estar na incubadora (OR: 3,2; IC 95%: 1,7–5,9) e baixo nível socioeconômico (OR: 2,4; IC de 95%: 1,1-5,2). 2) Setenta e três estudos observacionais foram incluídos (72 na meta-análise). Havia cinco diferentes critérios diagnósticos validados. A prevalência geral bruta de anquiloglossia foi de 4% (IC95%: 3% - 4%) variando de 67% para o critério de Coryllos (IC95%: 40% - 94%) a 2% para estudos que usaram critérios próprios (2%; IC95% : 2% - 2%). A prevalência foi similar entre faixas etárias e sexos. Entretanto, meninos tiveram 1,29 mais risco de ter anquiloglossia do que meninas (95%IC: 1,04-1,59) com muito baixa certeza de evidência. **Conclusão:** 1) Recém-nascidos prematuros e com BPN foram mais propensos a ter pérolas de Epstein e mucocele do que RN à termo e com peso normal. Amamentação e anquiloglossia não foram associadas à prematuridade e BPN. A prematuridade também foi associada à gravidez de alto risco, estar na incubadora e baixo nível socioeconômico. 2) A prevalência de anquiloglossia geral foi baixa, e maior para critérios diagnósticos validados comparado aos critérios próprios usados pelos autores. A prevalência de anquiloglossia foi semelhante para grupos de idade e sexo. Com muita baixa certeza da evidência, não podemos afirmar que meninos têm mais anquiloglossia que meninas.

Palavras-chave: Lesão de mucosa oral. Anomalias congênitas. Prematuridade. Baixo peso. Alto risco gestacional. Frênulo lingual. Anquiloglossia.

ABSTRACT

The relationship of prematurity and low birth weight with oral mucosal lesions in newborns and prevalence of ankyloglossia according to diagnostic criteria

Objective: This thesis describes two studies with the following objectives: 1) one cross-sectional study that aimed to associate prematurity and birth weight with the occurrence of oral mucosal lesions in newborns and associated factors, and 2) one systematic review that evaluated the prevalence of ankyloglossia in babies, children and adolescents according to different diagnostic criteria. **Methods:** 1) In the cross-sectional study, the sample comprised 431 pairs of mothers and newborns born at the University Hospital of Federal University of Minas Gerais. The study included mothers and newborns present in the hospital from August 2016 to April 2017. We excluded newborns with congenital anomalies or syndromes. A trained and calibrated dentist examined the mouth of the newborns for oral mucosal lesions (Kappa = 0.90). The lesions evaluated were dental lamina cysts, Bohn's nodules, Epstein's pearls, mucocele and ankyloglossia. Mothers answered a self-administered questionnaire related to socioeconomic indicators and prenatal habits. Medical records were evaluated to collect information about prematurity, low birth weight (LBW), pregnancy, childbirth, postpartum, maternal and newborn health conditions. Bivariate and multivariate logistic regression were used for data analysis. The level of significance was 5%. 2) For the systematic review, nine electronic databases were searched from interception up to May 2021 with no restrictions imposed regarding on year of publication or language. Paired independent reviewers selected studies, extracted data, and assessed the risk of bias. Using random-effects meta-analysis, we pooled the crude prevalence of ankyloglossia in general and by sex. Using mixed effect-meta-analysis, we subgrouped by diagnostic criteria and age. We calculated the PR and 95%CI of the occurrence of ankyloglossia in boys compared to girls, and assessed the certainty of evidence using the GRADE approach. **Results:** 1) Prematurity and LBW were associated with Epstein pearls (odds ratio [OR]: 1.7; 95% confidence interval [CI]: 1.03–3.0; OR: 1.8; 95%CI: 1.1–3.2, respectively) and mucocele (OR: 4.6; 95%CI: 1.3–16.1; OR: 3.7; 95%CI: 1.1–13.1, respectively), but not to ankyloglossia (OR: 1.0; 95%CI: 0.5–2.1; OR: 0.7; 95%CI: 0.3–1.6, respectively) or breastfeeding (OR: 0.5; 95%CI: 0.1-2.1; OR: 1.9; 95% CI: 0.2– 15.6, respectively). Prematurity was associated to high-risk pregnancy (OR: 2.3; 95% CI: 1.3–3.9), being in the incubator (OR: 3.2; 95% CI: 1.7–5,) and low socioeconomic status (OR: 2.4; 95% CI: 1.1-5.2). 2). 2) Seventy-three observational studies were included in the systematic review (72 in the meta-analysis). There were five different validated diagnostic criteria for ankyloglossia. The overall crude prevalence of ankyloglossia was 4% (95%CI: 3%-4%) varying from 67% for Coryllos criteria (40%-94%) to 2% for those studies using own criteria (2%; 95%CI: 2%-2%). There was a similar prevalence for age groups and both sexes. Boys had 1.29 more risk of having ankyloglossia (95%CI: 1.04-1.59) with very low certainty. **Conclusion:** 1) Preterm and LBW newborns were more likely to have Epstein pearls and mucocele than full terms. Breastfeeding and ankyloglossia were not associated with prematurity and

LBW. Prematurity was also associated with high-risk pregnancy, being in the incubator and low socioeconomic status. 2) The prevalence of ankyloglossia varied among all instruments used; with validated diagnostic criteria showing higher prevalence and non-validated or own criteria showing low prevalence. With low certainty, we could not affirm that boys are more prone to have ankyloglossia compared to girls.

Keywords: Oral mucosal injury. Congenital anomalies. Prematurity. Low birth weight. High gestational risk. Lingual frenulum.

LISTA DE FIGURAS

MANUSCRITO

APPENDIX

LISTA DE TABELAS

LISTA DE QUADROS

APPENDIX

LISTA DE ABREVIATURAS E SIGLAS

Em Português:

ABEP	Associação Brasileira das Empresas de Pesquisa
BP	Baixo Peso
BPN	Baixo Peso ao Nascer
CAAE	Certificado de Apresentação para Apreciação Ética
CAPES	Coordenação de Aperfeiçoamento de Pessoal de Nível Superior
CNPq	Conselho Nacional de Desenvolvimento Científico e Tecnológico
CNS	Conselho Nacional de Saúde
COEP	Comitê de Ética em Pesquisa com Seres Humanos
EBSERH	Empresa Brasileira de Serviços Hospitalares
FAPEMIG	Fundação de Amparo à Pesquisa do Estado de Minas Gerais
HC-UFMG	Hospital das Clínicas da Universidade Federal de Minas Gerais
IBGE	Instituto Brasileiro de Geografia e Estatística
IC	Intervalo de Confiaça
IG	Idade Gestacional
IST	Infecção Sexualmente Transmissível
NPBP	Nascidos Prematuros de Baixo Peso
OMS	Organização Mundial de Saúde
PIB	Produto Interno Bruto
PRPq	Pró-Reitoria de Pesquisa
RN	Recém-Nascido
RNT	Recém-Nascido a Termo
RNPT	Recém-Nascido Pré-Termo
RR	Risco Relativo
SUS	Sistema Único de Saúde
TCLE	Termo de Consentimento Livre e Esclarecido
UFMG	Universidade Federal de Minas Gerais
UTIN	Unidade de Tratamento Intensivo Neonatal

Em Inglês:

SE	Effect Estimate
GRADE	*Grading of Recommendations, Assessment, Development and Evaluation*
g	*grams*
HIV	*Human Immunodeficiency Virus*
IC	*Confidence Interval*
LBW	*Low Birth Weight*
NICU	*Neonatal Intensive Care Unit*
OR	*Odds Ratio*
PR	*Prevalence Ratio*
RR	*Relative Risk*
SD	*Standard Deviation*
WHO	*World Health Organization*

SUMÁRIO

1 CONSIDERAÇÕES INICIAIS

A Organização Mundial de Saúde (OMS) define os nascidos vivos de acordo com a idade gestacional em: recém-nascidos a termo, recém-nascidos pré-termo e recém-nascidos pós-termo. Os recém-nascidos pré-termo (RNPT) são aqueles nascidos com idade gestacional inferior a 37 semanas. Podem ser subdivididos de acordo com a idade gestacional em: pré-termo extremo (<28 semanas), muito pré-termo (28 a <32 semanas) e pré-termo moderado ou tardio (32 a 36 semanas e 6 dias) (WHO, 2018).

Recém-nascidos a termo (RNT) são aqueles com idade gestacional entre 37 e 41 semanas e 6 dias e pós-termo quando o nascimento ocorrer em um período igual ou superior a 42 semanas (CRUVINEL e PAULETTI, 2009; WHO, 2018). Além da idade gestacional, os nascidos vivos ainda podem ser classificados quanto ao peso apresentado ao nascimento. Baixo peso (BP) ao nascimento é definido quando inferior a 2.500 gramas, muito baixo-peso quando inferior a 1.500 gramas e extremo baixo-peso quando inferior a 1.000 gramas. Os determinantes do BP podem ser considerados o curto período gestacional ou a restrição de crescimento intrauterino, ou ainda a combinação dos dois fatores (WHO, 2018).

Além de afetar o desenvolvimento de órgãos e tecidos, o nascimento prematuro também pode afetar o desenvolvimento craniofacial e a cavidade bucal (SEOW e WAN, 2000). Ainda não existe um consenso sobre a etiologia para o nascimento prematuro de baixo peso (NPBP). Alguns fatores maternos vêm sendo associados às causas deste evento, porém não explicam completamente a ocorrência de partos prematuros. São eles: alterações sistêmicas, colo do útero curto, histórico de prematuridade e baixo peso em gestações anteriores, condição socioeconômica, raça, presença de infecções e hábitos deletérios (álcool, fumo e tabaco) (KRAMER *et al*., 2000). Portanto, a prevenção e identificação dos fatores de risco do NPBP devem ser voltadas para proporcionar um menor impacto na saúde materna e do recém-nascido (RN) (PEDRAZA *et al*., 2014).

No período pós-nascimento, o aspecto da cavidade bucal dos bebês se apresenta de forma singular e característica a esse período. Durante a infância, a cavidade bucal exibe um constante desenvolvimento, juntamente

com os demais sistemas e órgãos, e apresenta estruturas anatômicas particulares a esse período transitório (SCHMITT *et al*., 2012).

Até os seis meses de vida, pode ser comum a ocorrência de alterações congênitas na cavidade bucal dos bebês (SANTOS *et al*., 2009). Essas alterações, em sua maioria, são benignas e não oferecem riscos ao bebê (SCHMITT *et al*., 1994). No entanto, em alguns casos, podem gerar desconforto durante a alimentação e/ou provocar o surgimento de lesões secundárias na mucosa oral, podendo ser necessária intervenção cirúrgica (MARINI *et al*., 2014). Os cistos de inclusão (nódulos de Bohn, pérolas de Epstein e cistos da lâmina dentária) e freio lingual com curta inserção (anquiloglossia) são sugeridas como as alterações ou anomalias mais frequentes em RNs (ABANTO *et al*., 2009; CRUZ *et al*., 2020).

Os cistos de inclusão, inicialmente descritos por Fromm (1967), se apresentam como pequenas pápulas, branco ou branco-amareladas, formadas por camadas concêntricas de queratina, comumente encontradas na cavidade bucal dos RNs. Esses cistos são transitórios e não necessitam de tratamento. São encontrados em grupos de dois a seis cistos ou isoladamente (GOMES *et al*., 2011). São classificados de acordo com sua localização na cavidade bucal em: 1) pérolas de Epstein - cistos de queratina encontrados na rafe média palatina. Estes cistos são considerados remanescentes embrionários do tecido epitelial que foram aprisionados ao longo da rafe palatina durante o período intrauterino. 2) nódulos de Bohn - se apresentam como múltiplos nódulos difusos encontrados no rebordo alveolar, podendo ser localizados nas faces vestibular ou lingual, classificados como glândulas mucosas e remanescentes embrionários. 3) cistos da lâmina dentária - localizados bilateralmente na linha do rebordo alveolar, próximo à região do primeiro molar. São descritos como compostos remanescentes da lâmina dentária, que após o desenvolvimento do dente, fixaram-se na mucosa do rebordo e se proliferaram formando pequenos cistos de queratina (MACHADO *et al.,* 2005).

Um estudo prévio demonstrou que as pérolas de Epstein são as lesões mais prevalentes (39%), seguido pelos nódulos de Bohn (19.9%) e cistos da lâmina dentária (5.6%) (CRUZ *et al*., 2020). Moreillon e Schroeder (1982) observaram que, durante o período embrionário, à medida em que ocorre o aumento da idade fetal, há uma crescente proliferação de cistos, até

que ocorra a involução. Portanto, quanto menor a idade gestacional ao nascer, maiores as chances de os cistos serem observados na cavidade bucal de RNs (CRUZ *et al*., 2020).

A mucocele é uma lesão benigna causada pelo rompimento dos ductos secretores das glândulas salivares de menores dimensões localizadas na mucosa do lábio em 75,0 a 80,0% dos casos. Normalmente acomete lábio superior e inferior, palato mole, mucosa julgal e trígono retromolar. Clinicamente sua consistência é flutuante à palpação e pode estar localizada mais profundamente ou superficialmente ao tecido conjuntivo. Quando profunda, é observada uma coloração semelhante à da mucosa, e quando superficial, apresenta-se translúcida ou azulada (STUANI *et al*., 2010). A prevalência dessa lesão é de 2,4% para cada 1000 casos (HUZAIFA e SONI, 2021).

A anquiloglossia é definida como uma limitação da elevação ou protusão da ponta da língua, causada pelo encurtamento do frênulo lingual (membrana que conecta a língua ao assoalho bucal). Essa membrana tem um importante papel no crescimento e desenvolvimento da cavidade bucal e maxilofacial. Pode afetar a respiração, posição dos dentes na arcada, o aleitamento materno, a deglutição e a fala (LISONEK *et al*., 2017; FERRÉS-AMAT *et al*., 2017; SRINIVASAN *et al*., 2019). Além do encurtamento do frênulo lingual, outras características clínicas comumente observadas para diagnóstico da anquilossia são: quando em repouso, a língua permanece baixa na cavidade oral; há a formação de um ”coração” no ápice lingual e a fixação do frênulo no ápice da língua pode ser visível a partir da crista alveolar inferior (FRANÇA *et al.,* 2020). Essa alteração pode afetar até 56,6% dos recém-nascidos (FERRÉS-AMAT *et al*., 2017) e pode variar de acordo com a população e os critérios utilizados para o diagnóstico (SEGAL *et al.,* 2017).

Mesmo com a alta prevalência, não existem critérios clínicos padronizados para o diagnóstico de anquiloglossia ou qualquer consenso que seja amplamente utilizado. Os dados de prevalência e tratamento são marcados por uma grande heterogeneidade no diagnóstico e na avaliação dos resultados (SEGAL *et al*., 2017; MESSNER *et al*., 2020). A falta de consenso reflete diretamente em lacunas relacionadas à falta de evidências concisas sobre o diagnóstico, conduta clínica e adequado tratamento (MESSNER *et al*.,

2020).

É indispensável orientar familiares e profissionais da saúde sobre as possíveis alterações e anomalias que podem se desenvolver na cavidade bucal dos RNs. Deve-se avaliar a necessidade de cirurgias em caso de freios e bridas que apresentem inserções inadequadas (SCHMITT *et al*., 2012).

Portanto, esta tese apresenta dois estudos, um estudo transversal e uma revisão sistemática. Os objetivos foram, respectivamente: 1) verificar a associação da prematuridade e baixo peso ao nascer com a ocorrência de lesões de mucosa oral em RNs e com outros fatores; e 2) avaliar a prevalência de anquiloglossia e se há variação na prevalência de acordo com o critério diagnóstico utilizado. Com os resultados, espera-se identificar possíveis fatores relacionados, com a idade gestacional e peso ao nascer e sua relação com a ocorrência de lesões orais em recém-nascidos. Os resultados desse estudo mostrarão as principais diferenças entre os principais critérios diagnósticos e se existe um consenso entre os mesmos e poderão orientar profissionais de saúde, na escolha de uma ferramenta mais adequada para a avaliação da anquiloglossia.

1.1 OBJETIVOS

1.1.1 Objetivo geral

1) Verificar a associação da prematuridade e o baixo peso ao nascer com a ocorrência de lesões de mucosa oral em RNs e com fatores sociodemográficos e relacionados à saúde materno-infantil;

2) Avaliar os critérios diagnósticos para anquiloglossia existentes na literatura e verificar se a prevalência dessa alteração pode variar de acordo com o critério utilizado.

1.1.2 Objetivos específicos

a) Verificar se existe associação entre lesões de mucosa oral e nascimentos prematuros;

b) Verificar se existe associação entre lesões de mucosa oral e nascimentos de baixo peso;

c) Analisar a condição de saúde materna durante o período gestacional e sua relação com a prematuridade e baixo peso ao nascer;

d) Avaliar a condição de saúde do RN e sua associação com a prematuridade e baixo peso ao nascer;

e) Observar se fatores socioeconômicos podem estar relacionados com a prematuridade e baixo peso ao nascer;

f) Verificar a prevalência de anquiloglossia em bebês, crianças e dolescentes através de uma revisão sistemática;

g) Avaliar se a prevalência de anquiloglossia varia de acordo com o protocolo de diagnóstico utilizado.

h) Avaliar a prevalência de anquiloglossia por grupos etários e sexo.

2 ARTIGO

Oral Mucosal Lesions in Newborns: Relationship with Prematurity, Low Birth Weight, and Associated Factors

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Abstract

Background: An increase in prematurity and low birth weight (LBW) has been observed worldwide, to which several factors may be associated. This cross- sectional study aimed to evaluate the relationship between gestational age and LBW with oral mucosal lesions in newborns, maternal health conditions, newborn health conditions, and socioeconomic levels. **Materials and Methods:** The sample was comprised of 431 pairs of mothers- newborns born from a high and medium complexity hospital (CAAE nº: 57295316.3.0000.5149). Maternal health conditions and childbirth information were collected through the medical records and mothers answered a questionnaire on socioeconomic indicators. Oral mucosal lesions were evaluated by oral clinical examination. Gestational age and birth weight were analyzed, together with oral mucosal lesions and related factors, through bivariate and multivariate logistic regression models (α = 5%). **Results:** Prematurity and LBW were associated with Epstein pearls (odds ratio [OR]: 1.7; 95% confidence interval [CI]: 1.03–3.0; OR: 1.8; 95% CI: 1.1–3.2, respectively) and mucocele (OR: 4.6; 95% CI: 1.3–16.1; OR: 3.7; 95% CI: 1.1–13.1, respectively), but not ankyloglossia (OR: 1.0; 95% CI: 0.5–2.1; OR: 0.7; 95% CI: 0.3–1.6, respectively) or breastfeeding (OR: 0.5; 95% CI: 0.1- 2.1; OR: 1.9; 95% IC: 0.2– 15.6, respectively). **Conclusion**: Preterm and LBW newborns were more likely to have Epstein pearls and mucocele than full terms. Breastfeeding and ankyloglossia were not associated with prematurity and LBW.

Keywords: Low birth weight, newborn, oral mucosal lesion, oral pathology, preterm birth

Introduction

Premature infants are those born with a gestational age of 36 weeks and 6 days or less. Low birth weight (LBW) is defined as a newborn with <2500 g.[1,2] These conditions may have short and long- term consequences on neonatal health.[3,4] The care offered throughout the gestational and postnatal period, for both mother and newborn, must consist of early identification of possible health risk factors.[5] Preterm birth can affect craniofacial complex structures,[6,7] since the shorter the gestational age at birth, the greater the risk of congenital changes.[8] Thus, oral clinical alterations in newborns are very common, such as inclusion cysts, mucocele, and ankyloglossia.[6- 9]

The inclusion cysts are classified according to their location: (1) Epstein pearls occur in the region of the mean palatine raphe, (2) Bohn's nodules occur on the buccal or lingual surfaces of the alveolar ridge, and (3) dental lamina cysts occur bilaterally on the maxillary or mandibular alveolar ridge.[10] Most of these alterations are rarely observed after the first month of life due to their inoculum and/or transitory character.[11] However, there are cases in which these cysts occur more severely, leading to the occurrence of secondary lesions in the oral mucosa, causing pain and difficulties during breastfeeding,[12] and consequently to early weaning.

Mucocele is a benign oral lesion commonly found in newborns and may be caused by mechanical trauma, resulting in the rupture of the secretory ducts of the salivary glands, which leads to the formation of a cystic cavity filled with mucus. Mucoceles can be found on the lips and cheeks, as well as on the floor of the mouth.[13]

Ankyloglossia is characterized when there is a shortening or thickening of the lingual frenulum. These characteristics can lead to a decrease in the free lingual portion, which in turn causes functional restriction, which may interfere with speech, in the position of the dental arches and teeth, although it does not seem to affect breastfeeding.[14-16]

Although oral mucosal lesions have been discussed previously, most studies are only descriptive.[10,11,12] Two studies evaluated the relationship between inclusion cysts and prematurity and LBW.[9,17] However, other types of oral mucosal lesions other than inclusion cysts were not analyzed. It is important that health professionals closely monitor pregnant women and the fetus during pregnancy, at all levels of complexity, to maintain the health of the newborn. Therefore, it is necessary to identify possible oral changes that may be associated with the general health condition of newborns and that may influence early weaning. Thus, our study aimed to evaluate the relationship between gestational age and LBW with oral mucosal lesions in newborns and associated factors.

Materials and Methods

This cross- sectional study was conducted at a University Hospital, a reference center in care for pregnant women under gestational risk, located in Belo Horizonte, Brazil.

Data were collected from August 2016 to April 2017, and the study was approved by the Human Research Ethics Committee of the Federal University of Minas Gerais (CAAE # 57295316.3.00005149). The inclusion criteria were: all mothers who were hospitalized at the time of data collection and their newborns of both sexes. The exclusion criteria were newborns with neurological disabilities, craniofacial anomalies, and heart disease at birth reported on the medical records. Those mothers who agreed to participate signed an informed consent form.

The sample size was calculated using a prevalence of 56.4% of oral mucosal lesions,[18] with a margin of error of 5% and a 95% confidence interval (CI). A minimum sample of 378 newborns was determined, and 20% were added to compensate for possible losses, generating an estimated final sample of 453 newborns.

A theoretical training exercise was performed through pictures of oral mucosal lesions, followed by an oral clinical examination in newborns who did not participate in the main study. Calibration was conducted by a gold standard, expert in pediatric dentistry. The kappa value was 0.90 for inter- examiner agreement between the examiner and the gold standard.

A pilot study was conducted with 10 pairs of mothers/newborns before the main study. Participants were selected at the same hospital where the main study was conducted. As there were no intercurrences at this stage and no changes were necessary, all participants were included in the main study. The questionnaire and clinical examinationss were adequate.

Oral mucosal lesions were clinically diagnosed by the calibrated examiner. The newborns were lying down in their hospital crib and the examiner used a sterile clinical mirror, cotton swab, and artificial headlight. A research assistant took notes during oral examinations. The research team used appropriate personal protective equipment. The evaluated oral mucosal lesions included: Epstein Pearls, dental lamina cysts, Bohn's nodules, ankyloglossia, and mucocele, as described elsewhere.[9]

Through newborn's medical records, we collected the following data: newborn's sex, gestational age, birth weight, presence of infections (parasitic and viral infectious diseases, such as candidiasis, syphilis, human immunodeficiency virus [HIV] and infections caused by maternal urinary tract infection), need to be in the incubator, and admission to a neonatal intensive care unit (NICU) before being examined at the rooming- in.

The mothers were approached by the researchers in their hospital beds in the

Rooming- in and filled a structured questionnaire with information on gestational habits, use of medications during pregnancy, history of previous diseases, and socioeconomic level (defined according to the monthly family income and the Brazilian minimum wage[9]). Data were also collected related to mothers through medical records: sexually transmitted infections (HIV, Syphilis), previous health changes (parasitic and viral infectious diseases, cancers, Diabetes Mellitus), type of childbirth (vaginal childbirth, cesarean birth), and high- risk pregnancy. High- risk pregnancy was collected through the medical records, defined by complications developed during pregnancy or pre- existing comorbidities during pregnancy.[4] The following conditions were considered high- risk pregnancy: diabetes mellitus, infectious diseases (HIV, Syphilis), anemia, hypertensive disorders (chronic hypertension, eclampsia, pre- eclampsia), cardiovascular disease, respiratory diseases, and changes in amniotic fluid volume (polyhydramnios/oligohydramnios).

The main variables were categorized as: birth weight (≥2500g; <2500g) and gestational age (full- term: ≥37 weeks; preterm: <37 weeks). The other variables were categorized as type of childbirth (vaginal childbirth/cesarean section), newborn sex (female/male), mother's age (up to 19 years; 20 to 35 years; 36 years and over), and socioeconomic level. The socioeconomic level was categorized as "high" and "low" according to the questionnaire of the standard criterion of economic classification of the Brazilian Association of Research Companies, as described elsewhere.[19] The other variables were dichotomized into "yes" for the presence of the condition and "no" for the absence of the condition.

Data were entered into the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY, USA: IBM Corp.). Data analysis included descriptive statistics (frequency distribution, mean, and standard deviation). Bivariate and multivariate logistic regression analyses were conducted to verify the association between preterm birth or birth weight and other variables. The quality of models was tested by the Hosmer–Lemeshow test. Model #1 (bivariate analysis), which included all variables, was not adjusted. Model #2 included all the independent variables with $P < 0.20$. For Model #3, we looked for a better fit model than Model #2, when appropriate.

Results

The final sample was comprised of 431 pairs of mothers/newborns. The response rate was 95% and only 5.0% of the sample was excluded from the study due to incorrect completion of the questionnaire. Seventy- three newborns (16.9%) were preterms and 69 (16%) were LBW. The mean maternal age was 27.3 years ± 7.12 (minimum = 15;

maximum = 59 years). Of the total of newborns, 54.1% were males, with an average of 3.0 ± 3.4 days of life. The minimum weight at birth was 1.690 kg and the maximum weight was 4.700 kg (mean = 3.056 kg ± 531.26 g). The minimum preterm birth was 33 weeks and the maximum full- term birth was 42 weeks (mean = 38.2 weeks ± 1.83).

Table 1 shows bivariate (Model #1) and multivariate (Models #2 and #3) analyses for comparison between preterm and full- term birth. Data for gestational age were missing on 13 of the medical records, and 418 newborns were included in this analysis. Model #1 showed that babies who were not breastfed (odds ratio [OR]: 0.5; 95% CI: 0.1–2.1) and who presented ankyloglossia (OR: 1.0; 95% CI: 0.5–2.1) were not associated with prematurity. NICU and incubator were collinear variables ($P < 0.001$), and NICU was removed from the final adjusted multivariate model (Model #3). The type of birth and previous health change was also removed for a better adjustment of the model (Hosmer and Lemeshow test- $P = 0.708$). Model #3 showed that newborns that had Epstein pearls had a 1.7- fold greater chance (OR: 1.7; 95% CI: 1.03–- 3.0) of belonging to the preterm group than did those without Epstein pearls. Newborns who presented mucocele had a 4.6- fold greater chance (OR: 4.6; 95% CI: 1.3–16.1) of belonging to the preterm group than those without mucocele. Also associated with high- risk pregnancy were prematurity (OR: 2.3; 95% CI: 1.3–3.9), being in the incubator (OR: 3.2; 95% CI: 1.7–5.9), and low socioeconomic status (OR: 2.4; 95% CI: 1.1–5.2).

Table 2 shows bivariate (Model #1) and multivariate (Models #2) analyses for birth weight. There were six missing pieces of data for birth weight on the medical records, and 425 newborns were included in this analysis. Breastfeeding (OR: 1.9; 95% CI: 0.2–15.6) and ankyloglossia (OR: 0.7; 95% CI: 0.3–1.6) were also not associated with LBW (Model 1). Model #2 included all variables with $P < 0.20$ in the bivariate analyzes (Model #1), and the Hosmer and Lemeshow test showed a good adjustment ($P = 0.969$). Thus, Model #2 showed that newborns with mucocele presented a 3.7- fold greater chance (OR: 3.7; 95% CI: 1.1–13.1) of belonging to the LBW group. Likewise, newborns with Epstein pearls presented a 1.8- fold greater chance (OR: 1.8; 95% CI: 1.1–3.2) of belonging to the LBW group, when compared to those newborns without these oral mucosal lesions.

Discussion

This study demonstrated that Epstein pearls and mucocele were more frequent oral mucosal lesions in preterm birth and LBW newborns. Preterm and LBW have a high collinearity[9] and present similar associated factors. As expected, the main problems arising from high- risk pregnancy are preterm birth and LBW. These factors are

unfavorable for postnatal newborn survival.[20] High- risk pregnancy comprises a wide range of clinical and obstetric conditions and may compromise the healthy course of pregnancy.[4,20,21] When there are one or more risk factors related to maternal and/or fetal factors, an interaction can be observed between systemic components leading to adverse pregnancy outcomes.[4,20,21] About 15% of pregnant women develop some type of complication during pregnancy. These pregnant women need specific care, as their health status directly influences the fetal health status.[20]

Some studies did not find a significant association between birth weight, gestational age, and oral inclusion cysts.[17,22- 24] Another study of 60 preterm and 60 term newborns found that oral inclusion cysts were not associated with prematurity and LBW, but were positively associated with increased gestational age and weight gain.[11] Studies have shown that premature birthcan affect craniofacial complex morphology,[6,7] and the shorter the gestational period presented at birth, the greater the risk of congenital changes.[17] Epstein pearls tend to disappear spontaneously soon after birth.[18] A possible hypothesis that justifies the association found in this study is that newborns did not complete adequate gestational weeks for full development and there was not enough time for the remission of these lesions, that is, the more premature the newborn, the greater the chance of Epstein pearls to be present.[9]

Mucocele was associated with prematurity and LBW in the present study. The etiology of mucocele is mainly due to trauma and subsequent obstruction of the salivary glands.[13] Many preterm and LBW infants may be hospitalized in neonatal units and use neonatal intubation. Prolonged or incorrectly placed neonatal intubation can cause palatal groove formation by pressure against the hard palate, infection, laryngeal or tracheal edema, tracheal stenosis, and vocal cord injuries. However, injuries to the oral mucosa are less frequent than injuries to the nasal mucosa.[25] However, our newborns did not undergo neonatal intubation through the oral cavity, but rather through the nose. Other possible causes of mucocele are problems due to breastfeeding,[13] in utero thumb sucking, damages in oral mucosa during the passage in the birth canal, and the use of forceps.[26] Moreover, newborns hospitalized at the NICU or at the incubator may be more manipulated than newborns that are discharged from the hospital right after birth. However, one case report showed that mucocele is not frequent in newborns,[27] although the data are not from an epidemiological study. Moreover, the present found a low frequency of mucocele (n = 14 cases, 3.4%).

In fact, preterm and LBW newborns were more hospitalized at the NICU and the incubator. When the health status of the newborn is affected as a result of complications related to maternal and/or fetal health, the newborn may need specific care at the NICU and/or incubator,[18] be it for weight gain, thermal regulation, or

cardiorespiratory stability.[28,29]

Ankyloglossia proved not to be associated with prematurity and LBW. In our study, the diagnostic criterion used was that proposed by Martinelli et al.[30] Language development occurs between the 8th and 11th week of gestational period. At this stage, the cells of the frenulum undergo apoptosis and migrate to the median portion of the lingual dorsum. When there is interference in this process, the condition of ankyloglossia is installed.[31] Its relation to breastfeeding is controversial. Some studies relate the occurrence of ankyloglossia to functional problems linked to milk sucking, swallowing, and weight gain.[32,33] Other studies do not support this association between ankyloglossia and breastfeeding.[16,34,35]

The difference in the distribution of preterm newborns and LBW in relation to full- term and NBW newborns can be considered a limiting factor in this study. Future studies should follow- up on newborns to consolidate the results found in this study.

Conclusion

Epstein pearls and mucocele more commonly occurred in preterm and LBW newborns. These lesions can be transient and do not present risks. However, it is necessary to know the clinical characteristics of these lesions so that appropriate management would be performed if clinical interventions are needed. In many cases, the health professional may not identify the Epstein pearls and mucocele more commonly occurred in preterm and LBW newborns. These lesions can be transient and do not present risks. However, it is necessary to know the clinical characteristics of these lesions so that appropriate management would be performed if clinical interventions are needed. In many cases, the health professional may not identify the presence of oral lesions in newborns or can misdiagnose them with other oral alterations. There may be situations where parents or caregivers may notice the presence of some oral mucosal lesions, resulting in their search for oral health care.[36]

The results found in this study emphasize the relevance of knowing adverse health problems in specific populations. There are situations where oral mucosal lesions can compromise the newborn’s performance during breastfeeding. This dysfunction can lead to early weaning.[37] Thus, future studies should investigate oral mucosal lesions as possible risk factors for early weaning.

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Conflicts of interest

There are no conflicts of interest.

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Table 1: Bivariate and multivariate association between gestational age and other variables.

	Gestational age		Model 1 No adjusted		Model 2 Adjusted		Model 3 Adjusted	
Variables	**Full term**	**Preterm**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Newborn sex								
Female	161(46.7)	31(42.5)	1	0.513	-	-	-	-
Male	184(53.3)	42(57.5)	0.8 (0.5-1.4)		-		-	
High-risk pregnancy								
No	219(63.7)	31(42.5)	1	**0.001**	1	**0.020**	1	**0.002**
Yes	124(36.3)	42(57.5)	2.3(1.4-3.9)		2.0(1.1-3.7)		2.3(1.3-3.9)	
Type of childbirth								
Vaginal childbirth	219(85.5)	37(14.5)	1	**0.040**	1	0.502	-	-
Cesarean birth	125(77.6)	36(22.4)	1.7(1.02-2.8)		1.2(0.6-2.1)		-	
Breastfeeding								
No	8(4.2)	3(4.2)	1	0.383	-	-	-	-
Yes	336(97.7)	69(95.8)	0.5(0.1-2.1)		-		-	
Incubator								
No	299(86.7)	46(63.0)	1	**<0.001**	1	**0.002**	1	**<0.001**
Yes	46(13.3)	27(37.7)	3.8(2.1-6.7)		2.7(1.4-5.1)		3.2(1.7-5.9)	
NICU*								
No	326(94.5)	59(80.8)	1	**<0.001**	1	**0.024**	-	-
Yes	19(5.5)	14(19.2)	4.7(1.9-8.5)		2.6(1.1-6.3)		-	
Infections in newborn								
No	319(93.0)	70(95.9)	1	0.369	-	-	-	-
Yes	24(7.0)	3(4.1)	0.5(0.1-1.9)		-		-	
Epstein pearls								
No	214(62.0)	35(47.9)	1	**0.027**	1	**0.031**	1	**0.038**
Yes	131(38.0)	38(52.1)	1.7(1.1-2.9)		1.8(1.1-3.2)		1.7(1.03-3.0)	
Dental lamina cistys								
No	325(94.2)	71(97.3)	1	0.299	-	-	-	-

Yes	20(5.8)	2(2.7)	0.4(0.1-2.0)		-		-	
Bohn's nodules								
No	275(79.7)	57(78.1)	1	0.755	-	-	-	-
Yes	70(20.3)	16(21.9)	1.1(0.5-2.0)		-		-	
Continuation of the Table 1								
Mucocele								
No	337(97.7)	67(91.8)	1	**0.017**	1	**0.013**	1	**0.017**
Yes	8(2.3)	6(8.2)	3.7(1.2-11.2)		4.9(1.3-17.8)		4.6(1.3-16.1)	
Ankyloglossia								
No	294(85.5)	62(84.9)	1	0.899	-	-	-	-
Yes	50(14.5)	11(15.1)	1.0(0.5-2.1)		-		-	
Mothers's age								
Up to 19 years	51(15.0)	9(12.3)	1	0.882	-	-	-	-
20 to 35 years	241(70.7)	56(76.7)	0.9(0.3-2.5)		-		-	
36 years and over	49(14.4)	8(11.0)	1.3(0.6-2.8)				-	
Previous health changes								
No	284(82.3)	54(74.0)	1	**0.102**	1	0.607	-	-
Yes	61(17.7)	19(26.0)	1.6(0.9-2.9)		1.1(0.6-2.3)		-	
Sexually transmitted infections								
No	312(90.4)	64(87.7)	1	0.477	-	-	-	-
Yes	33(9.6)	9(12.3)	1.3(0.6-2.9)		-		-	
Socioeconomic level								
High	89(25.9)	9(12.3)	1	**0.016**	1	**0.040**	1	**0.026**
Low	255(74.1)	64(87.7)	2.4(1.1-5.1)		2.2(1.03-4.9)		2.4(1.1-5.2)	

Results in bold type are statistical significant at 5% level.
Logistic regression model with robust variance for multivariate analyses (Models #1, 2, and 3).
Model 1: robust model not adjusted.
Model 2: all variables with p<0.20 in the bivariate analyzes were included in this model. The Hosmer and Lemeshow test was performed (p=0.467).
Model 3: Type of birth, NICU and previous health change were removed from the analysis for a better adjust of the model. The Hosmer and

Lemeshow test was performed (p=0.708).
*NICU: intensive care units; OR - Odds ratio; CI – Confidence interval

Table 2: Bivariate and multivariate association between birth weight and other variables.

	Birth weight		Model 1 No adjusted		Model 2 Adjusted	
Variables	**≥2500g**	**<2500g**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Newborn sex						
Female	166(84.3)	31(15.7)	1	0.795	-	-
Male	190(83.3)	38(16.7)	0.9(0.5-1.5)		-	
High-risk pregnancy						
No	223(87.8)	31(12.2)	1	**0.009**	1	**0.048**
Yes	133(78.2)	37(21.8)	2.0(1.1-3.3)		1.7(1.006-3.1)	
Type of childbirth						
Natural childbirth	227(86.6)	35(13.4)	1	**0.040**	1	0.443
Cesarean birth	128(79.0)	34(21.0)	1.7(1.02-2.8)		1.2(0.7-2.2)	
Breastfeeding						
No	10(2.8)	1(1.4)	1	0.519	-	-
Yes	344(97.2)	68(98.6)	1.9(0.2-15.6)		-	
Incubator						
No	304(85.9)	50(72.5)	1	**0.010**	1	0.390
Yes	52(73.2)	19(26.8)	2.2(1.2-4.0)		1.3(0.6-2.7)	
NICU*						
No	339(86.3)	54(13.7)	1	**<0.001**	1	**<0.001**
Yes	17(53.1)	15(49.9)	5.5(2.6-11.7)		4.9(2.1-11.4)	
Infections in newborn						
No	331(83.8)	64(16.2)	1	0.819	-	-
Yes	23(82.1)	5(17.9)	1.1(0.4-3.0)		-	
Epstein pearls						
No	222(86.4)	35(13.6)	1	**0.072**	1	**0.032**
Yes	134(79.8)	34(20.2)	1.6(0.9-2.7)		1.8(1.1-3.2)	
Dental lamina cistys						
No	336(83.6)	66(95.7)	1	0.670	-	-
Yes	20(87.0)	3(13.0)	0.7(0.2-2.6)		-	
Bohn's nodules						

No	284(83.5)	56(16.5)	1	0.793	-	-
Yes	72(84.7)	13(15.3)	0.9(0.4-1.7)		-	

Continuation of the Table 2

Mucocele						
No	348(84.7)	63(15.3)	1	**0.011**	1	**0.040**
Yes	8(57.1)	6(42.9)	4.1(1.3-12.3)		3.7(1.1-13.1)	
Ankyloglossia						
No	303(83.2)	61(16.8)	1	0.476	-	-
Yes	53(86.9)	8(13.1)	0.7(0.3-1.6)		-	
Mothers's age						
Up to 19 years	55(87.3)	8(12.7)	1	0.453	-	-
20 to 35 years	244(81.6)	55(18.4)	0.6(0.1-2.0)		-	
36 years and over	54(91.5)	5(8.5)	1.5(0.6-3.4)		-	
Previous health changes						
No	287(84.7)	52(15.3)	1	0.321	-	-
Yes	69(80.2)	17(19.8)	1.3(0.7-2.4)		-	
Sexually transmitted infections						
No	323(84.3)	60(15.7)	1	0.339	-	-
Yes	33(78.6)	9(21.4)	1.4(0.6-3.2)		-	
Socioeconomic level						
High	93(90.3)	10(9.7)	1	**0.042**	1	0.070
Low	262(81.6)	59(18.4)	2.0(1.02-4.2)		1.9(0.9-4.2)	

Results in bold type are statistical significant at 5% level.
Logistic regression model with robust variance for multivariate analyses (Models #1 and 2).
Model 1: robust model not adjusted.
Model 2: all variables with p<0.20 in the bivariate analyzes were included in this model. The Hosmer and Lemeshow test was performed (p=0.969).
*NICU: Neonatal intensive care units; OR - Odds ratio; CI – Confidence interval

3 MANUSCRITO

PREVALENCE OF ANKYLOGLOSSIA ACCORDING TO DIFFERENT DIAGNOSTIC CRITERIA: SYSTEMATIC REVIEW

SHORT RUNNING TITLE: PREVALENCE OF ANKYLOGLOSSIA ACCORDING TO DIFFERENT CRITERIA

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AUTHOR CONTRIBUTIONS

PVC and CCM contributed to the study design. PVC, IGPO-A, ACS-O, RMM, SQN and CCM performed the data acquisition and analysis, selection of studies and data extraction. PVC and CCM contributed to the data interpretation and manuscript writing. CCM, PVC and CBB contributed to the critical revision of the manuscript. All authors read and approved the final version.

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CONFLICT OF INTEREST

The authors declare no conflict of interests.

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Abstract

Background: Ankyloglossia is a congenital anomaly characterized by the shortening of the lingual frenulum causing motor and functional problems, which the prevalence may vary according to the diagnosis. **Aim:** to evaluate the prevalence of ankyloglossia in babies, children, adolescents according to different diagnostic criteria. **Design:** In this systematic review and meta-analysis (PROSPERO #CRD42021224934), data were obtained from nine electronic databases, from interception up to May 2021 with no restrictions imposed regarding on year of publication or language. Paired independent reviewers selected studies, extracted data, and assessed the risk of bias. Using random-effects meta-analysis, we pooled the crude prevalence of ankyloglossia, subgrouped by diagnostic criteria, sex and age. We calculated the RR and 95%CI of the occurrence of ankyloglossia in boys compared to girls, and assessed the certainty of evidence using the GRADE approach. **Results:** Seventy-three observational studies were included (72 in the meta-analysis). There were five different validated diagnostic criteria. The overall crude prevalence of ankyloglossia was 4% (95%CI: 3%-4%) varying from 67% for Coryllos criteria (40%-94%) to 2% for those studies using their own criteria (2%; 95%CI: 2%-2%). There was a similar prevalence for age groups and both sexes. Boys had 1.29 more chances of having ankyloglossia (95%CI: 1.04-1.59) with very low certainty. **Conclusions:** There was a variation in the prevalence of ankyloglossia among all instruments used, with validated diagnostic criteria showing higher prevalence and non-validated or own criteria showing low prevalence.

KEYWORDS: lingual frenulum, tongue-tie, lip-tie, congenital abnormalities, clinical protocols.

1 | INTRODUCTION

The lingual frenulum is a small submucosal band of connective tissue that is inserted along the lower surface of the tongue to the oral floor.[1] Ankyloglossia, or "tongue-tie", is a congenital anomaly characterized by the shortening of the lingual frenulum or when the genioglossus muscle is highly adhered, limiting or restricting the movements of the tongue and causing motor and functional problems.[2,3] It is believed that the restriction of the tongue movement may influence breastfeeding, however this statement remains inconclusive.[4,5,6] Breastfeeding difficulties can also be related to pain in the mother's nipples.[2,3] In addition, ankyloglossia may affect the speech, swallowing and cause orthodontic problems including malocclusion, open bite and separation of the lower incisors.[6-8]

There is still no consensus on the diagnostic criteria for ankyloglossia, [4] although the diagnosis of ankyloglossia, it's treatment and difficulties in breastfeeding have grown exponentially in recent years.[9] According to observational studies carried out previously, the prevalence of ankyloglossia varies from 0.02% to 32.5%.[10-13] This prevalence may vary according to the population and the criteria used for the diagnosis.[13]

The data of prevalence have a great heterogeneity regarding the diagnosis and the evaluation of the results. There is no standard clinical criteria for the diagnosis of ankyloglossia or any consensus that is widely used which can explain the large range of prevalence.[13,14] The lack of a consensus directly reflects the gaps related to the lack of concise evidence about the diagnosis, clinical conduct and adequate treatment.[14] There is no prevalence of this condition compiled by systematic reviews grouping all possible prevalence studies. We found a methodological review that aimed to review the diagnostic criteria, prevalence and treatment of ankyloglossia.[13] However, this study has some limitations, it dates 2007, only two databases were searched and included only five studies that assessed the prevalence of ankyloglossia. Thus, a new systematic review is justified.

This systematic review is original and important for the clinical practice as it brings the prevalence of ankyloglossia considering all broad of available studies and diagnostic criteria. There are national health services that indicate surgical treatment if ankyloglossia causes problems. However, these bodies of evidence do not indicate the use of standardized diagnostic criteria.[6] This fact contributes to the great inconsistency of the prevalence data present in the literature. This review can also help the researchers who want to use the prevalence for sample calculation according to the diagnostic criteria that they intend to use in their studies. Finally, the objective of this systematic review was to evaluate the prevalence of

ankyloglossia in the population, and verify whether the prevalence of this alteration can vary according to the diagnostic criteria used.

2 | MATERIALS AND METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis 2020 (PRISMA) statement checklist was used for conducting and reporting this review.[15]

2.1 | Eligibility criteria

The clinical question was: what is the prevalence of ankyloglossia among newborns, infants, children and adolescents?

We included observational studies (cross-sectional and cohort) that evaluated the prevalence of ankyloglossia using any diagnostic criteria (validated or not). No restrictions were imposed on year of publication or language. We excluded adults; individuals submitted to frenectomy or treatment before diagnosis of ankyloglossia in interventional studies; studies not reporting prevalence of ankyloglossia; case-control studies; clinical trials; cases reports / cases series, reviews, letters to the editor and editorials.

2.2 | Information sources and search strategy

We searched nine electronic databases from interception up to May 2021: MedLine (through Ovid), Embase (through Elsevier), Scopus, Web of science, Cochrane Database of Systematic Reviews, Latin-American and Caribean Library (Lilacs) and the Brazilian Library of Dentistry (BBO) through the Virtual Health Library (Bireme, Latin America). Gray literature was searched through OpenGrey and Proquest Dissertation & Abstracts. We manually searched the reference list of selected articles to find any reference that could have been lost during the search in electronic databases. Each database had a specific search strategy previously prepared and verified by an expert in systematic reviews. The search strategies are presented in Appendix Table 1.

2.3 | Study selection

Studies were retrieved in EndNote software (EndNote® version 7.0 for Mac) and all duplicate references were removed. Five independent reviewers organized in pairs (PVC, IGPO-A, ACS-O, RMM and SQN) selected studies, first by titles and abstracts, then by full texts. Before each phase, reviewers underwent a training process carried out by the lead author with a sample of 10% of studies.

Initially, articles were screened by title and abstract. If the article met the inclusion criteria in the title /abstract, the full text was retrieved for further selection. Disagreements in all phases were solved by discussion and consensus. If disagreements persisted, sixth reviewer (CCM) was consulted.

2.4 | Data extraction

Data was extracted by five paired independent reviewers using a spreadsheet created in Microsoft Excel. The extracted data were: study design, language, continent of the authors, year of publication, setting of data collection, age of participants, initial and final sample, sex, difficulty in speech or breastfeeding or maternal nipple pain or dysphagia, number of individual with ankyloglossia, diagnostic criteria, description of the diagnostic criteria, funding and conflict of interest declared.

2.5 | Methodological quality

The independent reviewers assessed the methodological quality for each study according to The Joanna Briggs Institute (JBI) Critical Appraisal tools for cross-sectional and cohort studies.[16] This tool assesses the methodological quality of a study and determines the extent to which the possibility of bias in design, methodological conduction and analysis. The JBI consists of nine domains. Each domain can be judged as "yes", "no", "not apply" and if the authors did not provide enough evidence to make a judgment, the domain was classified as "unclear". Disagreements were discussed until a consensus was reached.

2.6 | Synthesis of results

The STATA software (version 12, StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP) was used to perform all meta-analysis. For meta-analysis of prevalence of ankyloglossia, we used random-effect model considering inherent

heterogeneity among different populations.[17] The I^2 statistic was used to analyzed the heterogeneity among the studies.

First, we performed a meta-analysis of pooled crude prevalence data. We extracted the final sample and number of individuals with ankyloglossia. One cohort study collected data in baseline and after one month of follow-up.[18] For the prevalence data, we included only baseline data as the sample was larger. Overall pooled crude prevalence and corresponding 95%CI were calculated. To explain the heterogeneity in the model, we run a random-effect meta-regression. The independent variable was year of publication, and the dependent variable was prevalence of ankylolgossia (using the pooled crude effect estimate).

Then, a subgroup meta-analysis was performed according to each diagnostic criteria and by age groups (babies, children and adolescents), as reported by authors, using mixed-effect model. For diagnostic criteria, we grouped "own criteria" and studies that "did not report the criteria" into a single group, considering both as non-validated criteria.

A pooled crude prevalence of ankyloglossia for boys and girls was also calculated through random-effect model, using the number of individuals with ankyloglossia per sex and overall sample.

As a secondary outcome, we investigated the occurrence of ankyloglossia between boys and girls. Total number of boys and girls and the number of individuals with ankyloglossia per sex was used to calculate prevalence ratio (PR) and corresponding 95%CI. Finally, we evaluated publication bias throught estimated log of the effect estimate (ES) in the funnel plot and Egger test.

2.7 | Certainty of evidence

We assessed the certainty of evidence for the risk of occurring ankyloglossia between boys and girls using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.[19]

Two independent reviewers (CCM and PVC) assessed the certainty of the evidence. Disagrements were resolved by consensus. The certainty of the evidence of observational studies starts with low.[19] The certainty can be downgraded due to problems of risk of bias, indirectness, imprecision, inconsistency, and publication bias. For observational studies, the certainty can be rated up due to magnitude of the effect, dose-response and residual confounders. Thus, the final certainty can be either very low, low, moderate, and high.[20] Finally, we presented the results in the Summary of Finding (SoF) Table created by

GRADEpro software (GRADEpro, available online at www.grade pro.org).

3 | RESULTS

3.1 | Study selection

From the searches conducted in the electronic databases, 3,350 articles were retrieved. After the duplicate studies were removed, 1,883 titles/abstracts were screened based on the eligibility criteria and 1,671 were excluded and 212 full texts were screened, 128 of which did not meet the eligibility criteria and 11 reports were not retrieved. Excluded studies and reasons for exclusion are in Appendix S1: Supplementary file. Therefore, 73 studies were included (Figure 1), being 72 cross-sectionals and one cohort. Seventy-two studies were included in the meta-analyses.

3.2 | Study characteristics

The characteristics of the 73 studies are listed in Table 1. The studies were published between 1975 and 2021, and 68.5% (50) of the studies were published after 2011. Ninety-four per cent of studies were published in English and 26% of authors are from South America. The total study sample comprised 36,013,869 babies, children and adolescents. Only 19.0% of the studies were funded by a government or university grant and 43.8% declared no conflicts of interest.

Thirty-four per cent of studies reported that the population had some type of difficulty in breastfeeding, speech, dysglossia, dysphagia or maternal nipple pain (Table 1). Thirty-seven per cent of studies used one or more validated criteria for the diagnosis of ankyloglossia; another 35.6% used non-validated diagnostic criteria (own criteria) and 27.4% did not report the type of criteria used (Appendix Table 2).

3.3 | Methodological quality

The methodological quality is reported in Appendix Figures 1 and 2. The major methodological problems of the studies included in the present review involved the representativeness of the sample (7.5%), sample size (62.5%) and problems in using non-valid and reliable methods to diagnose ankyloglossia (63.8%).

3.4 | Meta-analysis

One study was excluded from meta-analysis because it reported prevalence equal to zero; this study used the author's own criteria.[21] Thus, we could meta-analyze 72 studies. In general, the prevalence of ankyloglossia was 4% (95% CI: 3%-4%) (Table 2; Appendix Figure 3). For subgroup analysis, the prevalence was higher when studies used some validated criteria compared to own criteria or not reported criteria (Table 2; Appendix Figure 4). The prevalence was higher for studies using the Coryllos criteria (67%, 95%CI: 40%-94%); followed by Kotlow's criteria (21%; 95%CI: 13%-30%), Lingual Frenulum Protocol for Infants (LFPI or Neonatal Tongue Screening Test which is derived from the LFPI) (13%, 95%CI: 6%-19%) and Bristol Tongue Assessment Tool (BTAT) (12%, 95%CI: 10%-14%), and the combination of Assessment Tool for Lingual Frenulum Function (ATLFF) with Coryllos criteria (28%, 95%CI: 26%-30%). The prevalence was low for studies using own criteria or not reported criteria (2%, 95%CI: 2%-2%). The description of diagnostic criteria are on Appendix Table 3.

In the meta-regression model, year of publication had no effect on the crude prevalence of ankyloglossia (R^2: -1.10%; Tau^2: 0.03291; Coefficient: 0.0000506; Standard Error (SE): 0.0000923; p-value: 0.585).

Thirty studies reported the prevalence of ankyloglossia per sex and were included in a meta-analysis (Appendix Figure 5, 6, 7). The prevalence of ankyloglossia was 1% for girls and boys (Table 3). The prevalence ratio was 1.29 for boys compared to girls (95%CI: 1.04-1.59) with very low certainty (SoF table 4 shows the criteria for assessing the certainty of the evidence). The publication bias was investigated using a funnel plot (Appendix Figure 8) and Egger's test (p=0.091) showed no publication bias for this effect estimate.

A subgroup analysis was performed for age (Appendix Figure 9). The pooled crude prevalence of ankyloglossia varied from 7% (95%CI: 7%-7%) for babies, 8% (95%CI: 6%-10%) for children to 4% (95%CI: 4%-5%) for children and adolescents (Table 3).

3.5 | Certainty of evidence

SoF Table 4 shows the certainty of the evidence for occurrence of ankyloglossia between boys and girls. The very low certainty of evidence shows uncertainty about the effect estimate.[22] There was very serious problems due to risk of bias and inconsistency.

4 DISCUSSION

The overall crude prevalence of ankyloglossia was low, and subgroup analysis proved to be higher for studies using validated diagnostic criteria compared to own criteria used by authors. The prevalence of ankyloglossia for boys and girls was similar, and it is unlikely that boys are more prone to have ankyloglossia compared to girls. In subgroup analysis by age, the prevalence was slightly higher in infants and children.

The criteria with the highest prevalence of ankyloglossia were the Coryllos, Kotlows, LFPI and BTAT criteria, successively. The low crude prevalence of ankyloglossia that we found corroborates with a previous methodological review and varies according to the diagnostic criteria. This review found a prevalence of 4.0% using ATLFF criteria and 10.7% when using own criteria[13]. In other studies, the prevalence of ankyloglossia ranged from 0.02% using own criteria[10] , 3.2% among inpatients to12.8% among outpatients, when using ATLFF.[11]

In our results, three studies evaluated the the prevalence of ankyloglossia using the Coryllos criteria.[23] However, two of these studies included populations with difficulties in speech[24,25] and one study included population with breastfeeding difficulties[26] that might have overestimated the prevalence that we found. Chandrasekaran et al. found an overall prevalence of 3.4% in the general population, and 80% of ankyloglossia among patients with speech problems.[24] Haham et al (2004) found a prevalence of 38% in babies with breastfeeding difficulties[26] and Walls et al. found a prevalence of 82.6% among 3 year old children with difficulties in speech.[25] The Coryllos criteria has four items to assess the severity of ankyloglossia and the authors suggest that parameters related to the mother and baby should also be assessed.[23] However, the assessment of ankyloglossia is based on subjective criteria. The tool may have overestimated the prevalence of ankyloglossia toghether with a selection of a population with speech problems and breastfeeding difficulties rather than the general population, which would justify the high prevalence found in our study.

We also found a high prevalence when ankyloglossia was dignosed using the ATLFF[27]. Two studies were included in this subgroup and did not report any specific difficulties in speech or breastfeeding in their populations.[12,28] While one study found a prevalence of 12%[28] of ankyloglossia, the high pooled prevalence may be due to the study of Maria-Enero et al.[12] This cross-sectional study assessed the prevalence of ankyloglossia in 1,332 neonates and assessed the appearance and the function of the tongue, whether the mother felt pain in her

nipples, and whether the newborn had trouble grasping the breast. Akyloglossia was associated with breastfeeding difficules which might explain the high prevalence of ankyloglossia of the neonates of this study (46.3%)[12] Knox suggested to avoid using ATLFF due to its high complexity and the large number of items to be marked during the assessment.[29] Another study pointed out a low agreement among examiners, especially in functional criteria, that can be a limiting factor for the use of this protocol.[30] Therefore, there is doubts if the ATLFF results are reliable enough to state whether children with ankyloglossia will present breastfeeding difficulties or not.[31]

The prevalence that we found, using the Kotlow criteria,[32] corroborates with the study developed by Villa et al, in which the prevalence of ankyloglossia in children aged 6 to 14 years-old was 22.6% using this diagnostic criteria.[30] The prevalence of ankyloglossia ranged from 4%[33] to 63.4%[34] among the six studies included in this subgroup. According to the authors, the Kotlow criteria presents objective measures for the classification of the anatomy of the lingual frenulum in relation to the length of the lingual frenulum and tongue of babies and teenagers up to 14 years of age.[32] The tool is based on evaluating the length in millimeters of the tongue, from the insertion of the lingual frenulum, at its base, to its end. However, the author himself reports some difficulty in identifying children with mild and moderate degree of ankyloglossia due to the flexibility of the oral floor, as most of them do not present speech alterations.[32]

Nine studies were included in the subgroup of LFPI and the prevalences ranged from 3%[35] to 33%.[36] Our final prevalence is similar the study of Lopes et al [37] that found 13% of interference of the frenulum in tongue movements among 190 full-term infants up to 2 days of age. The LFPI is divided into three parts: clinical history; anatomical-functional evaluation and evaluation of non-nutritive sucking and nutritive sucking. The three parts of this protocol have independent scores and are simple to apply, so each part can be applied independently of one another until up to the 6th month of the baby's life. The tool is aimed to be objective to apply and can be used according to the objectives of the oral exam. For neonatal screening, in the first 48 hours after birth, usually only the anatomical and functional assessment of the baby is carried out for the diagnosis of ankyloglossia.[36]

Previous studies conducted with newborns assessed the anatomic-functional of the frenulum using the BTAT.[35,38,39] The prevalence of ankyloglossia was 12%[35] using BTAT, 3.1% using a combination of BTAT with LFPI[38] and 4% using a combination of BTAT with ATLFF.[39] The BTAT is a clinical practice-based tool that was created with reference to other assessment methods (ATLFF). This tool allows an objective, simple and clear measure of the severity of

ankyloglossia and the characteristics of the lingual frenulum.[40] Because it is objective and easy to apply, the professionals can be easly tranined in this tool for a greater agreement between examiners.

By the other side, the lack of a defined criteria reported by authors may have influenced the low prevalence in the "own criteria" subgroup. Some studies that did not use a valid criteria for ankyloglossia aimed to investigate several oral problems in children, such as Epnstein's pearls, Bohn's nodules, mucocele[41], geographic tongue and others[21], not only ankyloglossia. By the other side, studies that used validated criteria were investigations focusing mainly on ankyloglossia.[27,32] This must help to explain the differences in prevalence.

The prevalence of ankyloglossia was similar between sexes. However, although our review have demonstrated more risk among boys, the certainty was very low. There were very serious problems of inconsistency of the meta-analysis due to statistically significant heterogeneity, differences in effect estimates among studies and lack of overlap in some confidence intervals.[42] Moreover, there were very serious problems due to the methodological limitations of the studies. In general, all studies had some methodological limitation, mainly, representativeness of cases and lack of a valid criteria to measure ankyloglossia.

The prevalence of ankyloglossia was slightly higher in babies and children. In our review, while we had 38 studies including only babies, two studies grouped only adolescents. So far, it remains unclear if a baby with ankyloglossia, and not treated, will remain the same condition until adolescence. No prospective study was found regarding this issue.

4.1 | Strengths and limitations

A possible limitation is the high heterogeneity found among studies. However, even when exploring the heterogeneity with subgroup analysis, the heterogeneity remained in some subgroups. By the other side, the heterogeneity in prevalence data is a common issue, due to the different populations, different age groups, and different the application of the diagnostic criteria. Moreover, all studies had some methodological limitation, and due to this problem, we did not perform a sensitivity analysis once all studies should be removed. We opted to downgrade certainty of the evidence in two levels due to risk of bias.[43] As a strength of the review, the publication bias was assessed by funnel plot and Egger test, showing no evidence of publication bias for boys compared to girls. This shows all the efforts made to cover all possible studies in the field. Im addition, we assessed the certainty of the evidence of the effect estimate between boys and girls, showing the high methodological rigor of our study.

So far, this is the first review that summarizes the prevalence of ankyloglossia according to the diagnostic criteria.

4.2 | Implications for the clinical practice and the research

This review can be used as a basis for carrying out sample calculation in future epidemiological studies. Authors might decide to choose the prevalence for each diagnostic criteria. In addition, the evidence found here highlights the inconsistencies and variations between the diagnostic criteria for ankyloglossia. Future studies should try to define the best diagnostic criteria among all and provide precise information about the need or not to treat ankyloglossia. Also, future prospective studies should evaluate if the ankyloglossia remains as the infant grows up.

5 | CONCLUSION

The prevalence of ankyloglossia was mainly low and varied among all the diagnostic criteria used. Also, the prevalence of ankyloglossia was lower when diagnosed by a non-validated criteria and higher when diagnosed by validated tools. The prevalence of ankyloglossia was slightly higher in children and babies compared to adolescents; and quite similar between boys and girls.

REGISTRATION AND PROTOCOL

The protocol was registered a priori at the PROSPERO database (#CRD42021224934). One change was made from the original protocol. We excluded case-control studies from the sample of included studies.

BULLET POINTS

- This study reports the prevalence of ankyloglossia according to different diagnostic criteria, helping the researcher to choose a more suitable tool for their research and providing data to be used as a basis for sample calculation for future epidemiological studies.
- Ankyloglossia may vary according to the diagnosis, and validated criteria resulted in higher prevalence compared to non-validated criteria.
- It is expected low prevalence of ankyloglossia for epidemiological studies using non-

specific diagnostic criteria for ankyloglossia.

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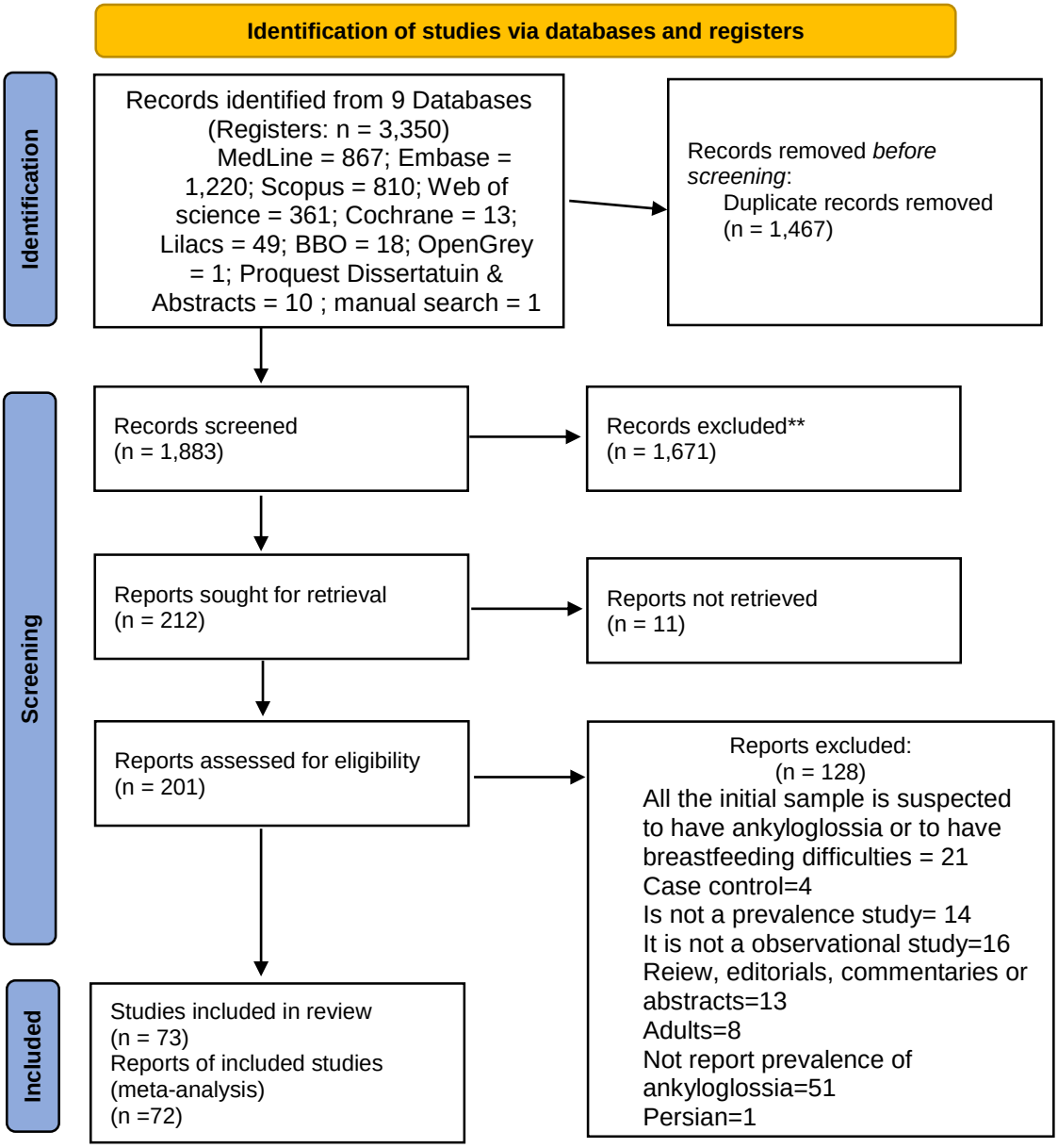

*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

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For more information, visit: http://www.prisma-statement.org/

Table 1. Summary of studies characteristics.

Characteristic	**Number 73 (100%)**
Language	
Portuguese	1 (1.4)
Spanish	3 (4.1)
English	69 (94.5)
Continents (authors from)	
Africa	3 (4.1)
Middle East	6 (8.1)
Europe	11 (15.0)
Asia	15 (21.3)
North America	13 (17.4)
South America	19 (26.0)
Collaboration between multi-countries	6 (8.1)
Year of publication	
1975 to 1994	7 (9.6)
2000 to 2010	16 (21.91)
2011 to 2021	50 (68.5)
Setting	
Orphanages	1 (1.4)
Re-education center	1 (1.4)
Home	2 (2.7)
Data base	4 (5.5)
Private clinic	6 (8.2)
School	14 (19.1)
Dental school/ hospital	43 (59.0)
Not reported	2 (2.7)
Funding	
Industry	2 (3.0)
Government/university grant	14 (19.0)
None	15 (20.5)
Not reported	42 (57.5)
Conflict of Interests	
The authors declare potential conflict of interests	1 (1.4)
The authors declare no conflict of interests	32 (43.8)
The authors do not report conflict of interests	40 (54.8)
Initial Sample	
Minimum	21
Maximum	32,140,679
Total	36,030,894
Final Sample	
Minimum	17
Maximum	32,140,679
Total	36,013,869
Sex	
Female	75,755 (47.7)
Male	83,223 (52.3)

Continuation of the Table 1	
Patient	
Babies	39 (53.4)
Children	7 (9.6)
Children and adolescents	24 (32.9)
Babies, children and adolescents	3 (4.1)
Difficulty type	
Dysglossia	1 (1.3)
Dysphagia	1 (1.3)
Difficulty in speech	5 (7.0)
Breastfeeding difficulties	12 (16.4)
Breastfeeding difficulties / Difficulty in speech	1 (1.3)
Breastfeeding difficulties / Maternal nipple pain	5 (7.0)
No difficulty	8 (10.9)
Not reported	40 (54.8)

Table 2. Pooled prevalence of ankyloglossia according to each diagnostic criteria.

Diagnostic criteria	**Number of Studies**	***I^2, P-value***	**ES (95%CI)**	**Mixed-effect* Z-test, p-value**
One criteria*				
Coryllos criteria	3	Not estimated	67% (40% - 94%)	4.94; <0.001*
Kotlow's criteria	7	98.8%, p<0.001	21% (13% - 30%)	4.90; <0.001*
Lingual Frenulum Protocol for Infants (LFPI)	10	98.7%, p<0.001	13% (6% - 19%)	3.86; <0.001*
Bristol Tongue Assessment Tool (BTAT)	1	Not estimated	12% (10% - 14%)	10.80; <0.001*
Assessment Tool for Lingual Frenulum Function (ATLFF)	3	Not estimated	3% (0% - 6%)	1.95; 0.05*
Use of more than one diagnostic criteria*				
ATLFF and Coryllos criteria	2	Not estimated	28% (26% - 30%)	30.77; <0.001*
ATLFF and BTAT	1	Not estimated	4% (2% - 8%)	2.50; 0.01*
LFPI and BTAT	1	Not estimated	3% (2% - 5%)	3.80; <0.001*
Own criteria or criteria not reported*	45	99.8%, p<0.001	2% (2% - 2%)	17.19; <0.001*
Overall prevalence**	72	99.8%, p<0.001; ***Tau^2:*** 0.00‡	4% (3% - 4%)	-

ES: effect estimate (prevalence); Mixed-effect model for subgroup analysis; **Random-effect model for overall prevalence; ‡*Tau^2* for overall pooled prevalence.

Table 3. Pooled prevalence of ankyloglossia by sex and age groups.

Diagnostic criteria	Number of Studies	I^2, *P-value*	Tau^2	ES (95%CI)	Mixed-effect* Z-test, p-value
Sex**					
Girls	30	97.2%, p<0.001	0.00	1% (1% - 1%)	-
Boys	30	98.1%, p<0.001	0.00	1% (1% - 2%)	-
Girls‡				PR: 1	
Boys‡	30	79.8%, p<0.01	0.1707	PR: 1.29 (1.04 – 1.59)	-
Age groups*					
Babies	39	99.6%, p<0.01	-	7% (7% - 7%)	31.68; <0.001*
Children	7	99.6%, p<0.01	-	8% (6% - 10%)	9.43; <0.001*
Adolescents	2	Not estimated	-	0% (0% - 1%)	2.45; 0.01*
Babies and children	1	Not estimated	-	0% (0% - 0%)	4.7; <0.001*
Babies, children and adolescents	2	Not estimated	-	0% (0% - 0%)	284.69; <0.001*
Children and adolescents	21	98.7%, p<0.01	-	4% (4% - 5%)	14.25; <0.001*
Overall**	72	99.8%, p<0.001	-	4% (3% - 4%)	-

ES: effect estimate (prevalence); *Mixed-effect model for subgroup analysis for age groups; **Random-effect model for overall prevalence. ‡Random effect meta-analysis of occurrence of ankyloglossia comparing girls versus boys; PR (prevalence ratio); Egger test for publication bias = p: 0.091, indication no publication bias.

Table 4: Summary of Finding (SoF): SoF table showing the effect estimate for ankyloglossia between boys and girls and the certainty of evidence.

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**boys**	**girls**	**Relative (95% CI)**	**Absolute (95% CI)**	
30	observational studies	very serious [a]	very serious [b]	not serious	not serious	none	1525/44858 (3.4%)	1237/40686 (3.0%)	**PR 1.29** (1.04 to 1.59)	**9 more per 1.000** (from 1 more to 18 more)	⨁◯◯◯ VERY LOW

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. The studies had very serious problems in varying topics of JBI tool, such as: representativeness of the target population, sample size, recruitment of the sample, coverage bias, reliability in the method used for diagnosis of ankyloglossia (e.g. non-validated criteria or not reported).
b. There were different effect estimates among studies, high statistically significant I^2.

4 CONSIDERAÇÕES FINAIS

Os resultados do presente estudo trazem informações sobre as lesões de mucosa oral mais comuns em RNs prematuros, com baixo peso ao nascer e sobre a prevalência de anquiloglossia em bebês, crianças e adolescentes de acordo com o critério. A necessidade de permanecer na incubadora e um menor nível socioeconômico estiveram diretamente relacionados ao parto prematuro. Já a necessidade permanência na UTIN, esteve relacionada apenas ao grupo de RNs com baixo peso ao nascer. Esses achados nos permitem concluir que o estado de saúde materno durante o período gestacional pode determinar ou interferir no estado de saúde fetal, podendo levar à prematuridade, baixo peso ao nascer e consequentemente ao desenvolvimento de doenças e à ocorrência de alterações na cavidade oral do RN.

As pérolas de Epstein e a mucocele foram mais comuns na presença de prematuridade e baixo peso ao nascer. No entanto, as alterações orais observadas neste estudo (Pérolas de Epstein, nódulos de Bohn, cistos da lâmina dentária, anquiloglossia e mucocele) também demostraram ser comuns tanto em RNs a termo, quanto em RNs pré-termo. Embora a etiologia dessas alterações ainda seja controversa, grande parte dos estudos sobre lesões de mucosa em RNs encontados na literatura odontológica são, em sua maioria, descritivos. Determinar os fatores gestacionais que influenciam no desenvolvimento de lesões de mucosa em RN, pode contribuir para um melhor entendimento da etiologia dessas lesões.

A prevalência geral de anquiloglossia variou de acordo com os critérios diagnósticos utilizados, semelhante em meninos e meninas, e ligeiramente maior em bebês e crianças.

É fundamental que haja uma interação interdisciplinar entre odontopediatras e pediatras. O conhecimento das características clínicas das alterações encontradas na cavidade oral de RNs e a utilização de critérios diagnósticos validados é fundamental para a seleção da conduta clínica adequada, caso sejam necessárias intervenções, e para orientação adequada aos responsáveis.

Os resultados deste estudo ressaltam a importância de se conhecer problemas adversos que podem interferir na saúde de gestantes. É necessário determinar estratégias adequadas para reduzir possíveis fatores de risco à saúde da gestante, com o objetivo de proporcionar uma melhor qualidade de vida durante o período gestacional à mulher e prevenir a ocorrência de nascimentos prematuros e BPN. Esses achados também evidenciam a necessidade da utilização de um critério diagnóstico padrão-ouro para maior confiabilidade dos diagnósticos realizados para a anquiliglossia. Estudos futuros que incluam uma amostra maior de RNs prematuros, de baixo peso ao nascer, mães com alto risco gestacional e que avaliem a acurácias dos critérios diagnósticos para a anquiloglossia são necessários para consolidar os resultados aqui apresentados.

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APÊNDICE A – Termo de consentimento livre e esclarecido (TCLE)

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Título da pesquisa: “Lesões de mucosa oral em recém-nascidos”
Local do estudo: Hospital das Clínicas

Pesquisador responsável: Poliana Valdelice Cruz, tel: 31 98821-5130

Email da pesquisadora: polianavcruz@gmail.com

Orientadora: Profa. Dra. Carolina Castro Martins, tel: 31 3409-2398

Coorientadora: Profa. Dra. Cristiane Baccin Bendo, tel: 31 3409-2432

COEP/ UFMG: (31) 3409 - 4592

Av. Antônio Carlos, 6627, Pampulha. Prédio da Reitoria, 7º andar sala 7018. CEP 31270-901

Convido a Sra._____responsável pelo bebê _____ a participar desta pesquisa que tem como objetivo relatar a ocorrência de lesões na boca dos recém-nascidos internados no Hospital das Clínicas, e observar quais fatores podem estar associados ao aparecimento dessas lesões. A pesquisa será realizada através de dados dos prontuários dos bebês e das mães, as mães responderão à um questionário, a boca do bebê será examinada. Os bebês que tiverem ou não alguma lesão terão a boca fotografada. As fotografias não mostrarão o rosto do bebê, somente o local da lesão será fotografado. As fotografias serão para fazer um registro e análise das lesões e poderão ser usadas somente para ciência, como artigos científicos, sem identificar o bebê. As fotografias serão armazenadas pelo pesquisador responsável pelo estudo, na Universidade Federal de Minas Gerais, pelo tempo pertinente ao estudo. Os exames da boca serão realizados nos bebês pela pesquisadora que usará luva de procedimento descartável, espelho clínico e abaixadores de madeira para língua. Este exame será feito utilizando-se todo o equipamento de proteção individual (luvas para procedimentos, óculos, gorro, máscara e avental) e com material descartável e/ou esterilizado. Este exame não oferece nenhum risco para o bebê. Os riscos serão mínimos, o bebê poderá chorar durante o exame, o que é considerado normal para a idade do seu filho.

Os dados analisados nesta pesquisa contribuirão para o diagnóstico e possíveis tratamentos das lesões da boca, além de orientar profissionais de saúde, mães e

familiares sobre o que fazer se essas lesões aparecerem na boca dos bebês. Os responsáveis pelos bebês participantes terão liberdade de retirar o consentimento a qualquer momento e deixar de participar da pesquisa sem que haja prejuízo ou danos ao atendimento no ambulatório. O (a) senhor (a) não terá qualquer tipo de despesa e nem receberá para participar da pesquisa. A identificação dos participantes da pesquisa será confidencial, assim como informações relacionadas à privacidade dos participantes. As informações serão utilizadas exclusivamente para estudo e pesquisa. Em caso de dúvidas éticas, o Comitê de Ética em Pesquisa da UFMG deverá ser consultado. Colocamo-nos à inteira disposição para resolver qualquer dúvida ou qualquer problema. Esta pesquisa está autorizada pelo Comitê de Ética em Pesquisa da UFMG (COEP). Qualquer dúvida ligue para o COEP, telefone (31) 3409 - 4592.

_____
Assinatura do pesquisador

Por este documento, eu, _____, autorizo a avaliação clínica do menor_____, nascido em ___/ ___/ _____, pelo qual sou responsável. Fui informada que receberei um questionário para responder. Dou minha permissão para que estes dados sejam utilizados para fins de pesquisa e ensino.

Belo Horizonte, _____ de _____de _____.

_____
Assinatura da mãe ou responsável

(Este termo encontra-se impresso em 02 vias, sendo que uma das vias ficará com o (a) senhor (a) e a outra será arquivada)

APÊNDICE B – Questionário

Faculdade de Odontologia
Universidade Federal de Minas Gerais
Departamento de Odontopediatria

Questionário

Por favor, responda ao questionário abaixo. Lembre-se, não há resposta certa ou errada; fique à vontade para responder da maneira que quiser. Suas respostas serão confidenciais. Agradecemos sua participação.

I. Identificação da mãe

1) Nome Completo:

_____

2) Nome no seu perfil do *Facebook*:

_____

3) Sua Data de Nascimento: ___/___/_____ Idade: _____

4) Endereço Completo: Rua:_____

nº_____

Bairro: _____ Cidade: _____Estado:

_____

CEP: _____-_____ Celular 1: (___)_____ Celular 2:

(___)_____

5) E-mail:

_____

6) Nome do

filho(a):_____

7) Data de Nascimento do Filho(a): ___/___/_____ Sexo: ( ) masculino ( )

feminino

II. Educação materna e paterna

8) Até que série <u>você</u> estudou?

( ) 1 a 4ª série incompleto
( ) 1 a 4ª série completo / 5 a 8ª série incompleto
( ) 5ª a 8ª série completo / Ensino médio incompleto
( ) Ensino médio completo / Superior incompleto
( ) Superior completo

9) Até que série <u>o pai do seu filho</u> estudou?

( ) 1 a 4ª série incompleto
( ) 1 a 4ª série completo / 5 a 8ª série incompleto
( ) 5ª a 8ª série completo / Ensino médio incompleto
( ) Ensino médio completo / Superior incompleto
( ) Superior completo

III. Condição socioeconômica

10) Quantas pessoas moram na sua casa? _____

11) Qual a renda mensal da sua família, incluindo auxílios do governo (ex: bolsa família, bolsa escola, etc.)?

( ) menos que R$ 880 ( ) R$ 880 a R$ 1759 ( ) R$ 1760 a R$ 2640
( ) R$ 2640 a R$ 3520 ( ) R$ 3520 a R$ 4400 ( ) mais que R$ 4400

12) Você ou algum membro da sua família recebe algum tipo de auxílio do governo? (Ex: bolsa família, bolsa escola, etc.)

( ) Sim. Valor: R$_____ ( ) Não

13) Você mora junto com o pai do bebê?

( ) Sim, casado/união estável ( ) Sim, não são casados mas moram juntos
( ) Não, nunca morou junto ( ) Não, são separados

Agora favor responder estas perguntas sobre itens do domicilio para efeito de classificação econômica. Todos os itens de eletroeletrônicos que foram citados devem estar funcionando, incluindo os que estão guardados. Caso não estejam funcionando, considere apenas se tiver intenção de consertar ou repor nos próximos seis meses.

14) Na sua casa tem? (favor marcar 0 quando não possuir)

	Quantidade
Automóveis (excluindo os de uso profissional)	( ) 0 ( ) 1 ( ) 2 ( ) 3 ( ) 4 ou +
Empregados mensalistas (que trabalhe pelo menos 5 vezes por semana)	( ) 0 ( ) 1 ( ) 2 ( ) 3 ( ) 4 ou +
Máquinas de lavar roupa (excluindo tanquinho)	( ) 0 ( ) 1 ( ) 2 ( ) 3 ( ) 4 ou +
Banheiros	( ) 0 ( ) 1 ( ) 2 ( ) 3 ( ) 4 ou +
Aparelhos de DVD (excluindo DVD de automóvel)	( ) 0 ( ) 1 ( ) 2 ( ) 3 ( ) 4 ou +
Geladeiras	( ) 0 ( ) 1 ( ) 2 ( ) 3 ( ) 4 ou +
Freezers	( ) 0 ( ) 1 ( ) 2 ( ) 3 ( ) 4 ou +
Microcomputadores (computadores de mesa, laptops, notebooks – excluindo	( ) 0 ( ) 1 ( ) 2 ( ) 3 ( ) 4 ou +

tablets, palms ou smartphones)	
Máquinas de lavar louça	( ) 0 ( ) 1 ( ) 2 ( ) 3 ( ) 4 ou +
Fornos micro-ondas	( ) 0 ( ) 1 ( ) 2 ( ) 3 ( ) 4 ou +
Motocicletas (excluindo as de uso profissional)	( ) 0 ( ) 1 ( ) 2 ( ) 3 ( ) 4 ou +
Máquinas de secar roupa (considerando também as que lavam e secam)	( ) 0 ( ) 1 ( ) 2 ( ) 3 ( ) 4 ou +

15) A água utilizada no seu domicílio é proveniente de?
( ) Rede geral de distribuição ( ) Poço ou nascente ( ) Outro meio

16) Há tratamento da água para beber?
( ) Filtrada ( ) Mineral ( ) Fervida
( ) Coada ( ) Sem tratamento ( ) Não sabe

17) Considerando a rua onde você mora, você diria que a rua é:
( ) Asfaltada/Pavimentada ( ) Terra/Cascalho

18) Quem é o chefe da família na sua casa? Considere como chefe da família a pessoa que contribui com a maior parte da renda do domicílio. (ex: você, marido, seu pai, sua mãe, etc.)
_____

19) Qual é o grau de instrução do chefe da família na sua casa?
( ) 1 a 4ª série incompleto
( ) 1 a 4ª série completo / 5 a 8ª série incompleto
( ) 5ª a 8ª série completo / Ensino médio incompleto
( ) Ensino médio completo / Superior incompleto
( ) Superior completo
( ) Não sei

IV – Saúde materna

20) Sua gravidez foi planejada? ( ) Sim ( ) Não

21) Quantas consultas de pré-natal foram realizadas? _____

22) Você recebeu orientações de higiene bucal nas consultas de pré-natal?
( )Sim ( ) Não ( )Não fiz pré-natal

23) Este é seu primeiro filho(a)? ( ) Sim ( ) Não

24) Com qual idade você teve seu primeiro filho(a)? _____

25) Você considera sua alimentação saudável durante a gravidez? ( ) Sim ( )Não

26) Durante a gravidez você exerceu algum tipo de trabalho?
( ) Não ( ) Sim
Qual trabalho?_____
___
Em qual período da gestação?
_____
Quantas horas/semana?_____

27) Durante a gravidez você teve algum tipo de problema (de saúde ou outro)?
( ) Pré-eclâmpsia ( ) Diabetes ( ) Pressão alta
( ) Outros: _____ ( ) Não tive problemas

28) Durante a gravidez você fez ingestão de álcool, drogas ou tabaco?
( ) Não ingeri ( ) Álcool ( ) Drogas ( ) Tabaco

29) Você possui alguma das doenças abaixo?
( ) Cardiopatia ( ) Hipertensão arterial ( ) Anemia
( ) Diabetes ( ) Não possuo comprometimento sistêmico

30) Você fez uso de algum medicamento durante a gestação?
( ) Não ( ) Sim. Qual(is)?
_____

V – Parto e aleitamento

31) Como foi o parto?
( ) Normal ( ) Normal com fórceps ( ) Cesariana ( ) Não sei

32) Houve traumas ou complicações durante o nascimento do(a) seu(sua) filho(a)?
( ) Não ( ) Sim. O que?_____

33) Você recebeu instruções sobre a amamentação do bebê? ( ) Sim ( ) Não

34) Seu filho(a) amamenta no peito? ( )Sim ( ) Não

35) Seu filho(a) usa mamadeira? ( ) Não ( ) Sim. O que você coloca na mamadeira?
_____
___

36) Quantas vezes por dia você amamenta seu filho(a)?
( ) Menos de 1 em 1 h ( ) De 1 em 1h ( ) De 2 em 2 h

( ) De 3 em 3h ( ) Mais de 3 em 3h

37) Se filho(a) tem dificuldades para mamar? ( )Não ( ) Sim. Por quê?_____.

38) Seu filho(a) usa chupeta (bico)? ( ) Sim ( ) Não ( ) Não, mas chupa o dedo

39) Caso seu filho(a) não use chupeta (bico), no futuro você pretende dar chupeta para o seu filho(a)?
( ) Não ( ) Sim Por que?
_____

40) Você já recebeu informações sobre a higiene bucal no seu filho(a)? ( ) Não ( ) Sim

Muito obrigada por ter respondido sinceramente todas as nossas questões!
Sua colaboração foi muito importante!

APÊNDICE C – Ficha Clínica Odontológica

Faculdade de Odontologia
Universidade Federal de Minas Gerais
Departamento de Saúde Bucal da Criança e do Adolescente

Ficha Clínica Odontológica

Nome do bebê: _____ Idade: _____dias

1- Aspecto geral da mucosa bucal: ( ) Normal ( ) Com alterações:_____

2- Apresenta alguma das alterações? ( ) Nódulos de Bohn ( ) Pérolas de Epstein ( ) Cistos de lâmina dentária ( ) Mucocele ( ) Dente natal ( ) Outro:_____

3- Região:_____.

4- Necessita de intervenções clínicas odontológicas? ( ) Sim ( ) Não

5- Há quanto tempo apresenta a alteração observada?_____.

6- Inserção do freio labial superior: ( ) Normal ( ) Com alterações_____

7- Inserção do frênulo lingual: ( ) Normal ( ) Com alterações_____

8 – Fixação do frênulo na face sublingual: ( )Terço médio ( )Entre terço médio e ápice ( )No ápice ( )Submerso

9- Aspecto da língua: ( ) Normal ( ) Saburra lingual ( ) Outras alterações:_____

Observações da pesquisadora:_____

_____

_____

_____

_____

_____

APÊNDICE D – Prontuário médico

Faculdade de Odontologia
Universidade Federal de Minas Gerais
Departamento de Odontopediatria

Prontuário Médico

Prontuário_____ Registro :_____
Data:_____/_____/_____

Nome:
_____

Data de nascimento: ____/___/___ Menarca: ____ Sexarca: ____ Parceiro fixo: _____

Religião:_____ Histórico familiar: _____

Alterações sistêmicas: _____

IST: _____

Uso de medicamentos: _____

Internações prévias: _____

Idade Gestacional:_____Data do parto:____/____/_____ Tipo de parto:_____

Gestação atual:_____( ) planejada ( ) não planejada e bem aceita ( ) não planejada e não aceita

Gestações
Anteriores:_____

Histórico de Aborto: _____Histórico de gemelaridade: _____

Nome do filho(a): _____Sexo: ( ) Masculino ( ) Feminino

Peso ao nascer: _____Comprimento:_____Perímetro cefálico:_____ Apgar: __/__

UTI: ( ) Não ( ) Sim. Quanto tempo?_____Por quê?_____

Incubadora: ( ) Não ( ) Sim. Quanto tempo?_____ Por quê? _____

Teve infecções? ( ) Não ( ) Sim.

Quais?_____

Medicação regularmente:_____

Outras anotações:
_____
_____
_____
_____

APÊNDICE E – Arquivo Suplementar: Revisão sistemática

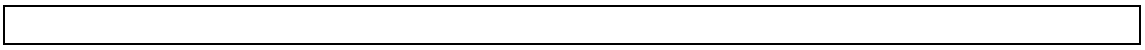
Suplemental Material

Appendix

Appendix Table 1. Search strategies used according to electronic databases (date: from interception to November 2020, updated on May 2021).

MedLine through Ovid
#1. ankyloglossia.mp. or exp Lingual Frenum/ or exp Ankyloglossia/
#2. tongue-tie.mp.
#3. exp Labial Frenum/ or lip-tie.mp.
#4. oral mucosal lesions.mp.
#5. oral lesions.mp.
#6. 1 or 2 or 3
#7. 1 or 2 or 3 or 4 or 5
#8. exp Prevalence/ or prevalence.mp.
#9. exp Cross-Sectional Studies/ or cross-sectional.mp.
#10. exp Diagnosis/ or diagnosis.mp.
#11. epidemiology.mp. or exp Epidemiology/
#12. incidence.mp. or exp Incidence/
#13. 8 or 9 or 10 or 11 or 12
#14. child*.mp. or exp Child/
#15. newborn*.mp. or exp Infant, Newborn/
#16. infant*.mp. or exp Infant/
#17. bab*.mp.
#18. 14 or 15 or 16 or 17
#19. frenectomy.mp.
#20. exp Ankyloglossia/ or Frenotomy.mp.
#21. 1 or 2 or 3 or 4 or 5 or 19 or 20
#22. 13 and 18 and 21

Embase through Elsevier #1. ankyloglossia #2. "tongue-tie" #3. "lip-tie" #4. “oral mucosal lesions” #5. “oral lesions” #6. frenotomy #7. frenectomy #8. prevalence #9. cross-sectional #10. diagnosis #11. epidemiology #12. incidence #13. child* #14. newborn* #15. infant* #16. bab* #17. #1 or #2 or #3 or #4 or #5 or #6 or #7 #18. #8 or #9 or #10 or #11 or #12 #19. #13 or #14 or #15 or #16 #20. #17 and #18 and #19
Scopus TITLE-ABS-KEY (ankyloglossia OR "tongue-tie" OR frenotomy OR frenectomy OR "oral mucosal lesions" OR "oral lesions") AND TITLE-ABS-KEY (prevalence OR cross-sectional OR diagnosis OR epidemiology OR incidence) AND TITLE-ABS-KEY (child* OR newborn* OR infant* OR bab*)
Web of science TS=((ankyloglossia OR "tongue-tie" OR “oral mucosal lesions” OR “oral lesions” or frenectomy OR frenotomy) AND (prevalence OR cross-sectional OR diagnosis OR epidemiology OR incidence) AND (child* OR newborn* OR infant* OR bab*))
Cochrane Systematic reviews #1. “ankyloglossia” #2. MeSH descriptor: [ankyloglossia] explode all trees #3. frenectomy #4. frenetomy #5. #1 or #2 or #3 or #4
Lilicas and BBO through Bireme (ankyloglossia) AND (diagnosis) AND (child* OR newborn*)
Proquest Dissertation & Abstracts (ankyloglossia or "tongue-tie" or “lip-tie” or frenetomy or frenectomy)
Open grey: 1 Ankyloglossia



Appendix S1: Supplementary file (References of excluded studies in the systematic review and reason for exclusion)

1.	Al-Maweri SA, Halboub ES, Al-Soneidar WA, Al-Sufyani GA. Oral lesions and dental status of autistic children in Yemen: A case–control study. J Int Soc Prev Community Dent 2014;4:S199-203.	The study does not report prevalence of ankyloglossia
2.	Amitai Y, Shental H, Atkins-Manelis L, Koren G, Zamir CS. Pre-conceptional folic acid supplementation: A possible cause for the increasing rates of ankyloglossia. Med Hypotheses 2020; 134:1-12.	case control
3.	Josefina JAN, Rodriguez-Archilla A. Oral mucosal lesions in patients of Mérida, Venezuela. Invest Clin 2015;56:367-376.	The study does not report prevalence of ankyloglossia
4.	Aras MH, Göregen M, Güngörmüş M, Akgül HM. Comparison of diode laser and Er: YAG lasers in the treatment of ankyloglossia. Photomed Laser Surg 2010;28:173-177.	It is not a observational study
5.	Ankur K, Bhasis JS, Baweja S. Tongue ties affecting breastfeeding in early term & full term neonates. Nutrition - Neonatal and infant nutrition.	Review, editorials, commentaries or abstracts
6.	Ata N, Alataş N, Yılmaz E, Adam AB, Gezgin B. The relationship of ankyloglossia with gender in children and the ideal timing of surgery in ankyloglossia. Ear Nose Throat J 2021;100:NP158-NP160.	All the initial sample is suspected to have ankyloglossia or to have breastfeeding difficulties
7.	Ataíde AP, Fonseca FP, Silva ARS, Júnior JJ, Lopes MA, Vargas PA. Distribution of oral and maxillofacial lesions in pediatric patients from a Brazilian southeastern population. Int J Pediatr Otorhinolaryngol 2016;90:241-244.	The study does not report prevalence of ankyloglossia
8.	Awa HDM, Mvondo RMN, Nguefack S, Messanga, CB, Ndombo POK. Les maladies rares et leurs manifestations cliniques orales dans deux formations hospitalières de Yaoundé. Pan Afr Med J 2019;32:195.	The study does not report prevalence of ankyloglossia
9.	Badawi N, Adelson P, Roberts C, Spence K, Laing, S, Cass D. Neonatal surgery in New South Wales—What is performed where? J Pediatr Surg 2003;38:1025-1031.	The study does not report prevalence of ankyloglossia
10.	Bajracharya D, Gupta S, Ojha B, Baral R. Prevalence	The study does

	of Oral Mucosal Lesions in a Tertiary Care Dental Hospital of Kathmandu. J Nepal Med Assoc 2017;56: 362-366.	not report prevalence of ankyloglossia
11.	Bamji MS, Sarma KR, Radhaiah G. Relationship between biochemical and clinical indices of B-vitamin deficiency. A study in rural school boys Br J Nutr 1979;41:431-441.	The study does not report prevalence of ankyloglossia
12.	Basra M, Patel N, Selbong UK. Tongue tie-Do we need to treat?. Br J Oral Maxillofac Surg 2019;57:e25.	It is not a observational study
13.	Bellinger V, Solari D, Hogan M, Rodda K, Shadbolt, B, Todd D. Tongue-tie division in the newborn: Follow-up at 9 and 38 months. Breastfeed Rev 2018;26:13–22.	All the initial sample is suspected to have ankyloglossia or to have breastfeeding difficulties
14.	Boras VV, Rogulj AA, Alajbeg I, Škrinjar I, Brzak BL, Brailo V et al. The prevalence of oral mucosal lesions in croatian children. Paediatr Croat 2013;57:235-238.	The study does not report prevalence of ankyloglossia
15.	Bronoosh P, Kasraeian M, Ghazi Saeedi B. Oral abnormalities in an Iranian newborn population. Pediatr Dent J 2014;24:8–11.	The study does not report prevalence of ankyloglossia
16.	Buck LS, Frey H, Davis M, Robbins, M, Spankovich, C, Narisetty V et al. Characteristics and considerations for children with ankyloglossia undergoing frenulectomy for dysphagia and aspiration. Am J Otolaryngol 2020;41:102393.	All the initial sample is suspected to have ankyloglossia or to have breastfeeding difficulties
17.	Bundogji N, Zamora S, Brigger M, Jiang, W. Modest Benefit of Frenotomy for Infants with Ankyloglossia and Breastfeeding Difficulties. Int J Pediatr Otorhinolaryngol 2020;133:109985.	All the initial sample is suspected to have ankyloglossia or to have breastfeeding difficulties
18.	Bundy M, Rogerson N, Dalal A, Kerr R, Finch G, Read K et al. Lingual frenectomy in infants and its effect on breastfeeding. Br J Oral Maxillofac Surg 2015;53:e75.	Review, editorials, commentaries or abstracts
19.	Caloway C, Hersh CJ, Baars R, Sally S, Diercks G, Hartnick CJ. Association of feeding evaluation with frenotomy rates in infants with breastfeeding	All the initial sample is suspected to

	difficulties. JAMA Otolaryngol. Head Neck Surg 2019;145:817-822.	have ankyloglossia or to have breastfeeding difficulties
20.	Carvalho IF, Alencar PNB, Carvalho de Andrade MD, Silva PGdeB, Carvalho EDF, Araújo LS et al. Clinical and x-ray oral evaluation in patients with congenital Zika Virus. J Appl Oral Sci 2019;27:e20180276.	The study does not report prevalence of ankyloglossia
21.	Chinnadurai S, Francis DO, Epstein RA, Morad A, Kohanim S, McPheeters M. Treatment of Ankyloglossia for Reasons Other Than Breastfeeding: A Systematic Review. Pediatrics 2015; 135:e1467–e1474.	Reiew, editorials, commentaries or abstracts
22.	Cawse-Lucas J, Waterman S, St Anna L. Clinical inquiry: does frenotomy help infants with tonguetie overcome breastfeeding difficulties? J Fam Pract 2015;64:126-127.	Reiew, editorials, commentaries or abstracts
23.	Chopra A, Lakhanpal M, Rao N, Gupta N, Vashisth S. Oral health in 4-6 years children with cleft lip/palate: A case control study. N Am J Med Sci 2014;6:27.	Case control
24.	Daggumati S, Cohn JE, Brennan MJ, Evarts M, McKinnon BJ, Terk AR. Caregiver perception of speech quality in patients with ankyloglossia: Comparison between surgery and non-treatment. Int J Pediatr Otorhinolaryngol 2019;119:70–74.	All the initial sample is suspected to have ankyloglossia or to have breastfeeding difficulties
25.	Dave J, Sinha V, Barot D, Modi N, Gurnani D,Patel T. Speech disorders encountered in routine ENT practice and the role of speech therapy in its effective management. Indian J Otol 2013; 19:169-172.	All the initial sample is suspected to have ankyloglossia or to have breastfeeding difficulties
26.	De Oliveira LJC, Torriani DD, Correa MB, Peres MA, Peres KG, Matijasevich A et al. Oral mucosal lesions' impact on oral health-related quality of life in preschool children. Commun Dent Oral Epidemiol. 2015;43:578–585.	The study does not report prevalence of ankyloglossia
27.	Díaz-Pizán ME, Lagravère MO, Villena R. Midline diastema and frenum morphology in the primary dentition. J Dent Child. 2006;73:11-14.	The study does not report prevalence of ankyloglossia
28.	Dixon B, Gray J, Elliot N, Shand B, Lynn A. A multifaceted programme to reduce the rate of tongue-tie release surgery in newborn infants: Observational	All the initial sample is suspected to

	study. Int J Pediatr Otorhinolaryngol 2018;113:156–163.	have ankyloglossia or to have breastfeeding difficulties
29.	Dollberg S, Manor Y, Makai E, Botzer E. Evaluation of speech intelligibility in children with tongue-tie. Acta Paediatr 2011;100:e125-e127.	The study does not report prevalence of ankyloglossia
30.	Dollberg S, Marom R, Botzer E. Lingual Frenotomy for Breastfeeding Difficulties: A Prospective Follow-Up Study. Breastfeed Medicin 2014; 9:286-289.	All the initial sample is suspected to have ankyloglossia or to have breastfeeding difficulties
31.	Dogenski LC, Farina AP, Linden MSS, Trentin MS, Miyagaki DC, De Carli JP. Oral Lesions found in a Dental School in Southern Brazil. J Contemp Dent Pract 2018;19:1037-1041.	The study does not report prevalence of ankyloglossia
32.	Dos Santos PJB, Bessa CFN, De Aguiar MCF, Do Carmo MAV. Cross-sectional study of oral mucosal conditions among a central Amazonian Indian community, Brazil. J Oral Pathol Medicin 2004;33:7-12.	The study does not report prevalence of ankyloglossia
33.	Douglas, P. 4 Preventing overdiagnosis in the first months of life. BJM Evidence-Based Medicine 2019;24:A1-A5.	Reiew, editorials, commentaries or abstracts
34.	Du RY, Mcgrath C, Yiu CKY, King NM. Oral health in preschool children with cerebral palsy: a case-control community-based study. International. J Paediatr Dent. 2010;20:330-335.	The study does not report prevalence of ankyloglossia
35.	Du RY, Yiu CK, King NM, Wong VC, McGrath CP. Oral health among preschool children with autism spectrum disorders: A case-control study. Autism 2014;19:746-751.	The study does not report prevalence of ankyloglossia
36.	Edmunds J, Hazelbaker A, Murphy JG, Philipp BL. Roundtable discussion: tongue-tie. J Hum Lactat 2012;28:14-17.	Reiew, editorials, commentaries or abstracts
37.	Edmunds JE, Fulbrook P, Miles S. Understanding the Experiences of Mothers Who Are Breastfeeding an Infant with Tongue-Tie. J Hum Lactat 2013;29:190-195.	The study does not report prevalence of ankyloglossia
38.	Ellehauge E, Jensen JS, Grønhøj C, Hjuler T. Trends of ankyloglossia and lingual frenotomy in hospital	All the initial sample is

	settings among children in Denmark. Danish Medic J 2020;67:A01200051.	suspected to have ankyloglossia or to have breastfeeding difficulties
39.	Erthal A, Lourenço SV, Nico MMS. Oral mucosal diseases in children - casuistics from the Department of Dermatology - University of São Paulo - Brazil. Braz Annals Dermatol 2016;91:849-851.	The study does not report prevalence of ankyloglossia
40.	Espinosa-Zapata M, Loza-Hernández G, Mondragón-Ballesteros R. Prevalence of buccal mucosa lesions in pediatric patients. Preliminary report. Cirug Cirujan 2006;74:153-157.	The study does not report prevalence of ankyloglossia
41.	Feng J, Zhou Z, Shen X, Wang Y, Shi L, Wang Y, , Shi L, Wang Y, Hu Y, Sun H, Liu, W. Prevalence and distribution of oral mucosal lesions: a cross-sectional study in Shanghai, China. J Oral Pathol Medic 2014;44:490-494.	The study does not report prevalence of ankyloglossia
42.	Ferres-Amat E, Pastor-Vera T, Ferres-Amat E, Mareque-Bueno J, Prats-Armengol J, Ferres-Padro E. Multidisciplinary management of ankyloglossia in childhood. Treatment of 101 cases. A protocol. Oral Med Oral Pathol Oral Surg 2016; 21:e39-e47.	All the initial sample is suspected to have ankyloglossia or to have breastfeeding difficulties
43.	Ferrés-Amat E, Pastor-Vera T, Rodriguez-Alessi P, Mareque-Bueno J, Ferrés-Padró E. The prevalence of ankyloglossia in 302 newborns with breastfeeding problems and sucking difficulties in Barcelona: a descriptive study. Eur J Paediatr Dent 2017;18:319-325.	All the initial sample is suspected to have ankyloglossia or to have breastfeeding difficulties
44.	Fletcher SG, Meldrum JR. Lingual Function and Relative Length of the Lingual Frenulum. J Spe Lang Hear Res 1968;11:382-390.	The study does not report prevalence of ankyloglossia
45.	França ECL, Albuquerque LCA, Martinelli RLC, Gonçalves IMF, Souza CB, Barbosa MA. Surface Electromyographic Analysis of the Suprahyoid Muscles in Infants Based on Lingual Frenulum Attachment during Breastfeeding. Int J Environment Res Pub Health 2020;17:859.	The study does not report prevalence of ankyloglossia
46.	Ghaheri BA, Cole M, Fausel SC, Chuop M, Mace JC. Breastfeeding improvement following tongue-tie and lip-tie release: A prospective cohort study. Laryngosc	All the initial sample is suspected to

	2016;127:1217-1223.	have ankyloglossia or to have breastfeeding difficulties
47.	Ghaheri BA, Cole M, Mace JC. Revision Lingual Frenotomy Improves Patient-Reported Breastfeeding Outcomes: A Prospective Cohort Study. J Hum Lactat 2018; 34:566-574.	All the initial sample is suspected to have ankyloglossia or to have breastfeeding difficulties
48.	Gheno JN, Martins MAT, Munerato MC, Hugo FN, Sant'ana Filho M, Weissheimer C, Carrard VC, Martins MD. Oral mucosal lesions and their association with sociodemographic, behavioral, and health status factors. Braz Oral Res 2015;29:1-6.	The study does not report prevalence of ankyloglossia
49.	Glynn RW, Colreavy M, Rowley H, Gendy S.. Division of tongue tie: Review of practice through a tertiary paediatric otorhinolaryngology service. Int J Pediatr Otorhinolaryngol 2012; 76:1434-1436.	All the initial sample is suspected to have ankyloglossia or to have breastfeeding difficulties
50.	Gopal RM. An observational study of tongue tie release using bipolar diathermy at vellore district in tamilnadu. J Evolut Med Dent Scienc 2018;7:5335-5339.	Is not a prevalence study
51.	Hale M, Mills N, Edmonds L, Dawes P, Dickson N, Barker D, Wheeler BJ. Complications following frenotomy for ankyloglossia: A 24‐month prospective New Zealand Paediatric Surveillance Unit study. J Paediatr Child Health 2020;56:557-562.	Is not a prevalence study
52.	Hall DMB, Renfrew MJ. Tongue tie. Arch Dis Child 2005;90:1211-1215.	Reiew, editorials, commentaries or abstracts
53.	Han SH, Kim MC, Choi YS, Lim JS, Han KT. A study on the genetic inheritance of ankyloglossia based on pedigree analysis. Arch Plast Surg 2012;39:329-332.	All the initial sample is suspected to have ankyloglossia or to have breastfeeding difficulties
54.	Hanna R, Parker S. The advantages of carbon	It is not a

	dioxide laser applications in paediatric oral surgery. A prospective cohort study. Las Medic Scien 2016;31:1527-1536.	observational study
55.	Harris EF, Friend GW, Tolley EA. Enhanced Prevalence of Ankyloglossia with Maternal Cocaine Use. Cleft Palate-Craniofac J 1992;29:72-76.	case control
56.	Harrison-Woolrych M, Paterson H, Tan M. Exposure to the smoking cessation medicine varenicline during pregnancy: a prospective nationwide cohort study. Pharmacoepidemiol Drug Safet 2013;22:1086-1092.	Is not a prevalence study
57.	Hasan A, Cousin G. Ankyloglossia (tongue-tie). Afr J Paediatr Surg 2015;12:101.	It is not a observational study
58.	Hazelbaker AK. Newborn tongue-tie and breast-feeding. J Americ Board Famil Pract 2005;18:326-326.	Reiew, editorials, commentaries or abstracts
59.	Tobey AH, Kozar AJ, FAOASM R. Frequency of Somatic Dysfunction in Infants With Tongue-Tie: A Retrospective Chart Review. The AAO 2017;10.	It is not a observational study
60.	Hurst N, Tucker K. Diagnosing ankyloglossia. J Hum Lactat 2013;29: 423-423.	Reiew, editorials, commentaries or abstracts
61.	Illing S, Minnee M, Wheeler J, Illing L. The value of frenotomy for ankyloglossia from a parental perspective. NZ Med J 2019;132:70-81.	Is not a prevalence study
62.	Janiszewska-Olszowska J, Gawrych E, Dydyk A, Studniak E, Biaduń-Popławska A, Zajączek S. Oro-palatal dysplasia Bettex–Graf – Clinical findings, genetic background, treatment. J Cranio-Maxillofac Surg 2013;41:e29-e32.	It is not a observational study
63.	Josefina JAN, Rodriguez-Archilla A. Oral mucosal lesions in patients of Mérida, Venezuela. Investig clinic 2015;56:367-376.	The study does not report prevalence of ankyloglossia
64.	Karabulut R, Sönmez K, Türkyilmaz Z, Demiroğullari B, Ozen IO, Bağbanci B, Kale N, Başaklar AC. Ankyloglossia and effects on breast-feeding, speech problems and mechanical/social issues in children. B-ENT 2008;4:81-85.	Is not a prevalence study
65.	Khoo AKK, Dabbas N, Sudhakaran N, Ade-Ajayi N, Patel S. Nipple Pain at Presentation Predicts Success of Tongue-Tie Division for Breastfeeding Problems. Eur J Pediatr Surg 2009;19:370-373.	Is not a prevalence study
66.	Kleinman DV, Swango PA, Pindborg JJ. Epidemiology of oral mucosal lesions in United States schoolchildren: 1986-87. Community Dentist Oral	The study does not report prevalence of

	Epidemiol 1994;22:243–253.	ankyloglossia
67.	Klockars T, Pitkäranta A. Pediatric tongue-tie division: Indications, techniques and patient satisfaction. Int J Pediatr Otorhinolaryngol 2009;73:1399-1401.	Is not a prevalence study
68.	Köse O, Güven G, Özmen İ, Akgün ÖM, Altun C. The oral mucosal lesions in pre-school and school age Turkish children. J Eur Academy Dermatol Venereol 2011;27:e136-e137.	The study does not report prevalence of ankyloglossia
69.	Legbo JN, Opara WE. Day-care plastic surgery in Nigeria: Coping with limited resources. Annals Afric Medic 2005;4:14-18.	Is not a prevalence study
70.	LeTran V, Osterbauer B, Buen F, Yalamanchili R, Gomez G. Ankyloglossia: last three-years of outpatient care at a tertiary referral center. I J Pediatr Otorhinolaryngol 2019;126:109599.	It is not a observational study
71.	Linares-Vieyra C, del Carmen Meza-Sánchez J, González-Guevara MB, Murrieta-Pruneda JF, Salgado-Rodríguez SJ, Morales-Jaimes R. Lesiones de mucosa bucal. Factores asociados en población infantil. Medic J Mexic Instit Soc Secur 2013;51:320-325.	The study does not report prevalence of ankyloglossia
72.	Lu HX, Tao DY, Lo ECM, Li R, Wang X, Tai BJ, et al. The 4th National Oral Health Survey in the mainland of China: background and methodology. Chin J Dent Res 2018;21:161-165.	The study does not report prevalence of ankyloglossia
73.	Machet L, Hüttenberger B, Georgesco G, Doré C, Jamet F, Bonnin-Goga B, et al. Absence of Inferior Labial and Lingual Frenula in Ehlers-Danlos Syndrome. Amer J Clinic Dermatol 2010;11:269-273.	The study does not report prevalence of ankyloglossia
74.	Marra PM, Itro A. Surgical Management of Frenula: Laser Therapy Compared with Z-Frenuloplasty Technique. Braz Res Pediat Dentist Integ Clin 2020;20:e0027.	It is not a observational study
75.	Martinelli RLDC, Marchesan IQ, Berretin-Felix G. Compensatory strategies for the alveolar flap production in the presence of ankyloglossia. J CEFAC. 2019;21:e10419	Sample of adults
76.	Martinelli RLDC, Marchesan IQ, Berretin-Felix G. Tongue position for lingual frenulum assessment. J CEFAC 2020;22:e0120.	Sample of adults
77.	McBride C. Tongue‐tie. J Paediatr Child Health 2005;41:242-242.	Reiew, editorials, commentaries or abstracts
78.	Miller AS, Miller JE. Is tongue tie really the problem? Incidence of ankyloglossia in an infant population presented with suboptimal feeding: a cross-sectional survey. J Clin Chiropr Pediatr 2017;16:1350-1354.	All the initial sample is suspected to have

		ankyloglossia or to have breastfeeding difficulties
79.	Molania T, Nahvi A, Delrobaee M, Salehi M. Frequency of Oral Mucosal Lesions and Awareness of these Lesions in Patients Attending Oral and Maxillofacial Clinic in Sari Dental School, Iran. J Mazand Univers Medic Sci 2017;26:80-87.	Language: Persian
80.	Muldoon K, Gallagher L, McGuinness D, Smith V. Effect of frenotomy on breastfeeding variables in infants with ankyloglossia (tongue-tie): a prospective before and after cohort study. BMC Pregn Childb 2017;17:373.	It is not a observational study
81.	Naimer SA, Biton A, Vardy D, Zvulunov A. Office treatment of congenital ankyloglossia. Med Sci Monit 2003;9:CR432-CR435.	It is not a observational study
82.	Neves M, do Amaral Giordani JM., Ferla AA, Hugo FN. Primary care dentistry in Brazil: From prevention to comprehensive care. JACM 2017;40:S35.	The study does not report prevalence of ankyloglossia
83.	Nolan C, Corry P, O'Rourke C, Fenton JE. To examine what percentage of patients referred to centre for tongue tie release were referred for breastfeeding difficulties and how many of them stopped breastfeeding as a result. Irish J Med Sci 2015;184:S165-S166.	reiew, editorials, commentaries or abstracts
84.	O'Callahan C, Macary S, Clemente S. The effects of office-based frenotomy for anterior and posterior ankyloglossia on breastfeeding. Int J Pediatr Otorhinolaryngol 2013;77:827-832.	It is not a observational study
85.	O'Leary CM, Slack-Smith LM. Dental hospital admissions in the children of mothers with an alcohol-related diagnosis: a population-based, data-linkage study. J Pediatr 2013;63:515-520.	The study does not report prevalence of ankyloglossia
86.	O'Shea JE, Foster JP, O'Donnell CP, Breathnach D, Jacobs SE, Todd DA, Davis PG. Frenotomy for tongue‐tie in newborn infants. Cochrane Database Syst Rev 2017;3:CD011065.	reiew, editorials, commentaries or abstracts
87.	Padilla CD, Cutiongco EM, Sia JM. Birth defects ascertainment in the Philippines. Southeast Asian J Trop Med Public Health 2003;34:239-43.	The study does not report prevalence of ankyloglossia
88.	Parlak A, Koybasi S, Yavuz T, Yesildal N, Anul H, Aydogan I, Kavak A. Prevalence of oral lesions in 13- to 16-year-old students in Duzce, Turkey. Oral Dis 2006;12:553–558.	The study does not report prevalence of ankyloglossia

89.	Pauws E, Moore GE, Stanier P. A functional haplotype variant in the TBX22 promoter is associated with cleft palate and ankyloglossia. J Med Genet 2009;46:555–561.	It is not a observational study
90.	Pereira NM, Maresh A. Trends in outpatient intervention for pediatric ankyloglossia. Int J Pediatr Otorhinolaryngol 2020;138:110386	The study does not report prevalence of ankyloglossia
91.	Navarro NP, López M. Anquiloglosia en niños de 5 a 11 años de edad: Diagnóstico y tratamiento. Rev Cubana Estomatol 2002;39:282-301.	It is not a observational study
92.	Periyasamy Y, Ravindran V, Subhashini VC.Oral mucosal lesions in children with and without cleft lip and palate: A case control study. Int J Res Pharm Sci 2020;11:1233-1238.	Case control
93.	Pinsak GF. A radiographic and model analysis of patients manifesting partial congenital ankyloglossia. Am J Orthod 1977;72:331–332.	review, editorials, commentaries or abstracts
94.	Praborini A, Setiani A , Munandar A, Wulandari R A.. A Holistic Supplementation Regimen for Tongue-Tied Babies With Slow Weight Gain and Failure to Thrive. Clin Lact 2018;9:78-87.	All the initial sample is suspected to have ankyloglossia or to have breastfeeding difficulties
95.	Pransky SM., Lago D, Hong P. Breastfeeding difficulties and oral cavity anomalies: The influence of posterior ankyloglossia and upper-lip ties. Int J Pediatr Otorhinolaryngol 2015;79:1714–1717.	All the initial sample is suspected to have ankyloglossia or to have breastfeeding difficulties
96.	Prasertsom P, Kaewkamnerdpong I,Krisdapong S. Condition-Specific Oral Health Impacts in Thai Children and Adolescents: Findings From the National Oral Health–Related Quality of Life Survey. Asia Pacif J Pub Health 2020;32:49-56.	The study does not report prevalence of ankyloglossia
97.	Pola M, Garcia MG, Martin JMG, Gallas M, Leston JS. A study of pathology associated with short lingual frenum. J Dent Child 2002;69:59-62.	It is not a observational study
98.	Potter NL, Bajwa A, Wilson EH, VanDam M. Developmental Changes in Tongue Strength, Swallow Pressures, and Tongue Endurance. Dysphag 2020;1-10.	Is not a prevalence study

99.	Qiao Y, Shi H, Wang H, Wang M, Chen F. Oral Health Status of Chinese Children With Autism Spectrum Disorders. Front Psych 2020;11:398.	The study does not report prevalence of ankyloglossia
100.	Ruffoli R, Giambelluca M, Scavuzzo M, Bonfigli D., Cristofani R, Gabriele M, Giannessi F. Ankyloglossia: a morphofunctional investigation in children. Oral Dis 2005;11:170–174.	Is not a prevalence study
101.	Guzmán LR, Quiroz TC, Bailón NR, Felices LR, Costa CP, Guiu CG. Herencia de la anquiloglosia: de tal palo, tal astilla. Rev Ped Aten Primar 2019;21:e129-35.	Is not a prevalence study
102.	Salt H, Claessen M, Johnston T, Smart S. Speech production in young children with tongue-tie. Int J Ped Otorhinolaryngol 2020;134:110035.	Is not a prevalence study
103.	Sandberg-Wollheim M, Neudorfer O, Grinspan A., Weinstock-Guttman B, Haas J, Izquierdo G, Coyle PK. Pregnancy outcomes from the branded glatiramer acetate pregnancy database. Int J MS Care 2018;20:9-14.	The study does not report prevalence of ankyloglossia
104.	Sedano JR, Arroyo IC, Muñoz MD, Romero CA., Carrera EM,Fraile AG. Anquiloglosia neonatal¿ Existe un exceso de indicación intervencionista. Acta Pediatr Esp 2016;74:45-9.	It is not a observational study
105.	Serrano-Martinez M, Bagan J, Silvestre F, Viguer M. Oral lesions in recessive dystrophic epidermolysis bullosa. Oral Dis 2003;9:264–268.	Sample of adults
106.	Sharma SD, Jayaraj S. Tongue-tie division to treat breastfeeding difficulties: our experience. J Laryngol Otol 2015;129:986–989.	All the initial sample is suspected to have ankyloglossia or to have breastfeeding difficulties
107.	Shenoy RP, Agrawal R, Salam TA, Shenoy KP. Screening for temporomandibular disorders and other oral conditions among adolescents in mangaluru taluk. World J Dent 2020;11:201-5	The study does not report prevalence of ankyloglossia
108.	Shulman JD. Prevalence of oral mucosal lesions in children and youths in the USA. Int J Paediatr Dent 2005;15:89–97.	The study does not report prevalence of ankyloglossia
109.	Solis-Pazmino, P, Kim GS, Lincango-Naranjo E., Prokop L, Ponce OJ, Truong MT. Major complications after tongue-tie release: A case report and systematic review. Int J Pediatr. Otorhinolaryngol 2020;110356.	It is not a observational study

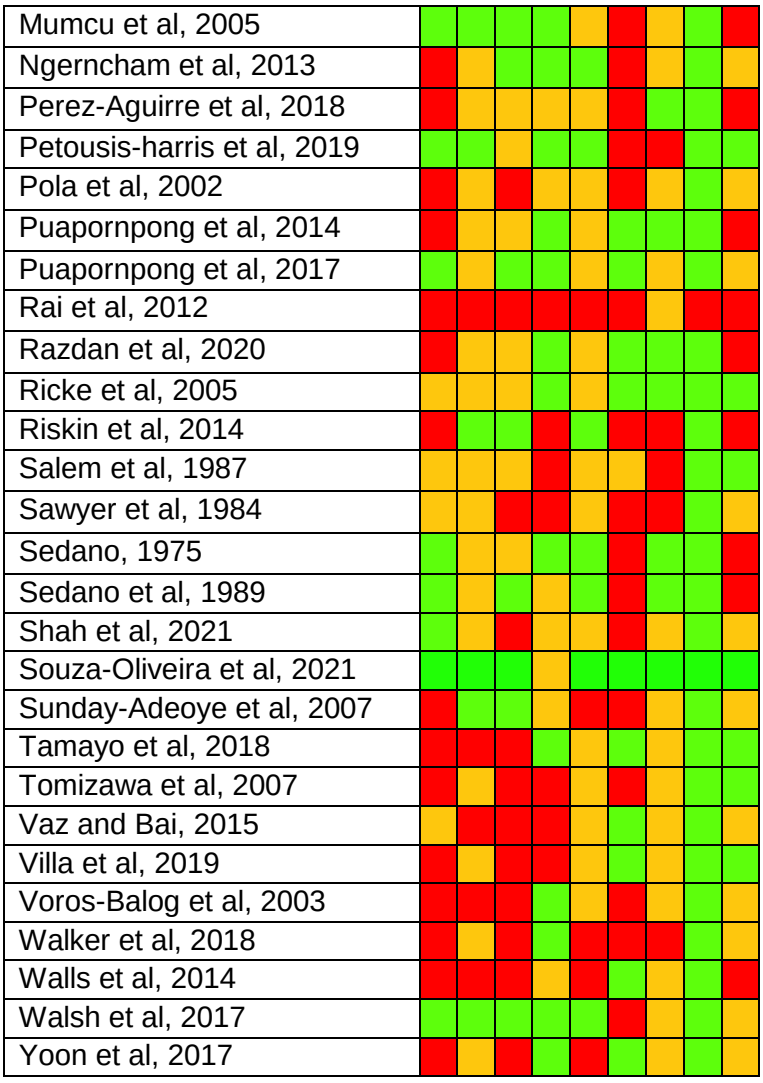
110.	Swain SK, Sahu MC, Choudhury J. Speech disorders in children: Our experience in a tertiary care teaching hospital in eastern India Ped Poli 2018;93:217-220.	Is not a prevalence study
111.	Taani, DSMQ. Oral health in Jordan. Int Dent J 2004;54:395-400.	The study does not report prevalence of ankyloglossia
112.	García AT. Prevalencia de lesiones bucales en tejido blando encontradas en la Clínica de Estomatología de la Facultad de Odontología de la Universidad de los Andes. Periodo 2015-2018. J ADM 2020;77:11-16.	Sample of adults
113.	Dabić DT, Kansky A, Boras VV. Prevalence of oral mucosal lesions in Slovenia. RJPBCS 2015;6:1154-7.	The study does not report prevalence of ankyloglossia
114.	Thapa P, Aryal KK, Dhimal M, Mehata S, Pokhrel AU, Pandit A, Pandey AR, Bista B, Dhakal P, Karki KB, Pradhan S. Oral Health Condition of School Children in Nawalparasi District, Nepal. RJPBCS 2015;13:7-13.	The study does not report prevalence of ankyloglossia
115.	Ünür M, Kayhan KB, Altop MS, Metin, ZB, Keskin, Y. The Prevalence of Oral Mucosal Lesions in Children: A Single Center Study. JIUFD 2015;49:29.	The study does not report prevalence of ankyloglossia
116.	Velten DB., Zandonade E, Miotto MHMB.. Prevalence of oral manifestations in children and adolescents with cancer submitted to chemotherapy. BMC Oral Health 2017;16:107.	The study does not report prevalence of ankyloglossia
117.	Vieira EMM. Estudo das condições de saúde bucal e avaliação da microbiota periodontopatogênica de uma população indígena brasileira 2009:115.	Sample of adults
118.	Vieira EM, Ciesielski FI, Gaetti-Jardim EC, Hespanhol D, Castro EV, Castro AL, Schweitzer CM, Jardim Júnior EG. Evaluation of oral health in a community of native Brazilians of the Umutina Reservation, Mato Grosso state. Int J Odontostomat 2011;59-63.	Sample of adults
119.	Vieira EMM, Salineiro FS, Hespanhol D, Musis, CR,. Junior EGJ. Frequência de anquiloglossia em uma comunidade indígena brasileira. Rev Gaúcha Odontol 2010;58:215-218.	Sample of adults
120.	Vieira-Andrade RG, Martins-Júnior PA, Corrêa-Faria P, Stella PEM, Marinho SA, Marques LS, Ramos-Jorge ML. Oral mucosal conditions in preschool children of low socioeconomic status: prevalence and determinant factors. Eur J Pediatr 2013;172:675–681.	The study does not report prevalence of ankyloglossia
121.	Wakhanrittee J, Khorana J,Kiatipunsodsai S. The	All the initial

	outcomes of a frenulotomy on breastfeeding infants followed up for 3 months at Thammasat University Hospital. Pediatr Surg Int 2016;32: 945-952.	sample is suspected to have ankyloglossia or to have breastfeeding difficulties
122.	Xu L, Han P, Liu Y, Wang H, Yang Y, Qiu F,Zhu Y. Study on the Effect of Kidney Transplantation on the Health of the Patients' Offspring: A Report on 252 Chinese Children. Cell Biochem Biophys 2013;68:173–179.	The study does not report prevalence of ankyloglossia
123.	Yin W, Yang YM, Chen H, Li X, Wang Z., Cheng L., Nie MH. Oral health status in Sichuan Province: findings from the oral health survey of Sichuan, 2015–2016. Int J Oral Sci 2017;9:10-15.	The study does not report prevalence of ankyloglossia
124.	Yin Y. Yu Z, Zhao M, Wang Y, Guan X. Comprehensive evaluation of the risk of lactational mastitis in Chinese women: combined logistic regression analysis with receiver operating characteristic curve. Biosci Rep 2020;40:BSR20190919.	Is not a prevalence study
125.	Yilmaz AE, Gorpelioglu C, Sarifakioglu E, Dogan DG, Bilici M, Celik NU. Prevalence of oral mucosal lesions from birth to two years. Niger J Clin Pract 2011;14:349-53.	The study does not report prevalence of ankyloglossia
126.	Yilmaz AE, Gorpelioglu C, Sarifakioglu E, Dogan DG, Bilici M, Celik NURULLAH. Prevalence of oral mucosal lesions from birth to two years. Niger J Clin Pract 2011;14:349-353.	The study does not report prevalence of ankyloglossia
127.	Yoon AJ, Zaghi S, Ha S, Law CS, Guilleminault C, Liu SY. Ankyloglossia as a risk factor for maxillary hypoplasia and soft palate elongation: A functional - morphological study. Orthod Craniofac Res 2017;20:237–244.	Sample of adults
128.	Zeng H, Cai H, Wang Y, Shen,Y. Growth and development of children prenatally exposed to telbivudine administered for the treatment of chronic hepatitis B in their mothers. IJID 2015;33:97–103.	The study does not report prevalence of ankyloglossia

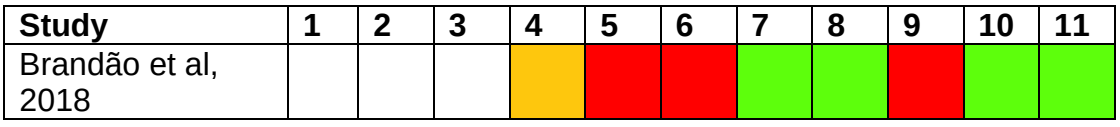
Appendix Table 2. Summary of diagnostic Criteria.

Diagnostic criteria	**Number of individuals with ankyloglossia**	**Number of Studies 73(100%)**
Lingual Frenulum Protocol for Infants (LFPI)	823	9 (12.3)
Kotlow's criteria	912	7 (9.6)
Coryllos criteria	466	3 (4.1)
ATLFF-Assessment Tool for Lingual Frenulum Function (ATLFF)	328	3 (4.1)
Non-validated diagnostic criteria	42,571	26 (35.6)
Diagnostic criteria not reported	82,659	20 (27.4)
Use of more than one diagnostic criterion		
LFPI and Bristol Tongue Assessment Tool (BTAT)	140	2 (2.7)
ATLFF and Coryllos criteria	82	1 (1.4)
Coryllos criteria and ATLFF	645	1 (1.4)
ATLFF and BTAT	6	1 (1.4)

Study	1	2	3	4	5	6	7	8	9
Ambika et al, 2011									
Araujo et al, 2020									
Bai and Anna, 2014									
Bandaru et al, 2019									
Basalamah and Baroudi, 2016									
Becerra-Culqui and Sy, 2020									
Campanha et al, 2019									
Çetinkaya et al, 2011									
Chandler et al, 2019									
Chandrasekaran et al, 2020									
Chang et al, 2020									
Chiang et al, 2014									
Cinar and Onat, 2005									
Da Silva Dal ben et al, 2008									
De Oliveira et al, 2019									
Do Rêgo et al, 2020									
Dutra et al, 2020									
Ekenze, 2005									
El-Bassyouni et al, 2019									
Flink et al, 1994									
Fonteles et al, 2018									
Freudenberger, 2008									
Friend et al, 1990									
Fujinaga et al, 2016									
Garcia-Pola, 2002									
Garcia-Pola MJ, 2002									
Haham et al, 2014									
Hipólito and Martins, 2010									
I Zen et al, 2020									
Jahanbani et al, 2012									
Jamilian et al, 2014									
Jiménez et al, 2014									
Jorgenson et al, 1982									
Kishore et al, 2017									
Krittika and Don, 2019									
Lisonek et al, 2017									
Livingstone et al, 2000									
Lopes et al, 2016									
Madera Anaya et al, 2013									
Majorana et al, 2010									
Martinelli et al, 2018									
Maya-Enero et al, 2021									
Messer et al, 2000									
Mohan et al, 2014									
Morisso et al, 2012									



Appendix Figure 1. Methodological quality of 72 prevalence studies. Low quality is represented in red; unclear is represented in orange; high quality of bias is represented in green.



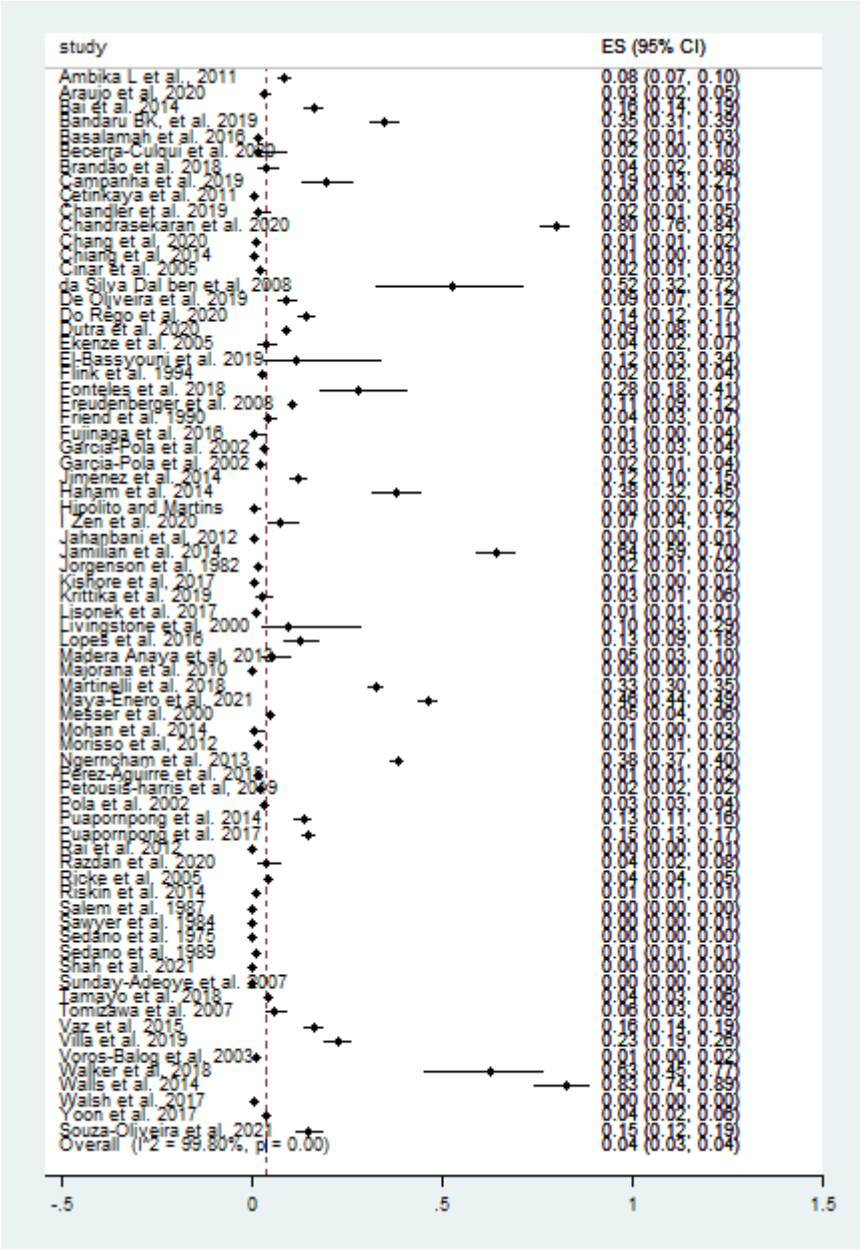
Appendix Figure 2. Methodological quality of one cohort study. Low quality is represented in red; unclear is represented in orange; high quality of bias is represented in green; criteria that do not apply is shown in white.

Appendix Table 3. Description of the diagnostic criteria

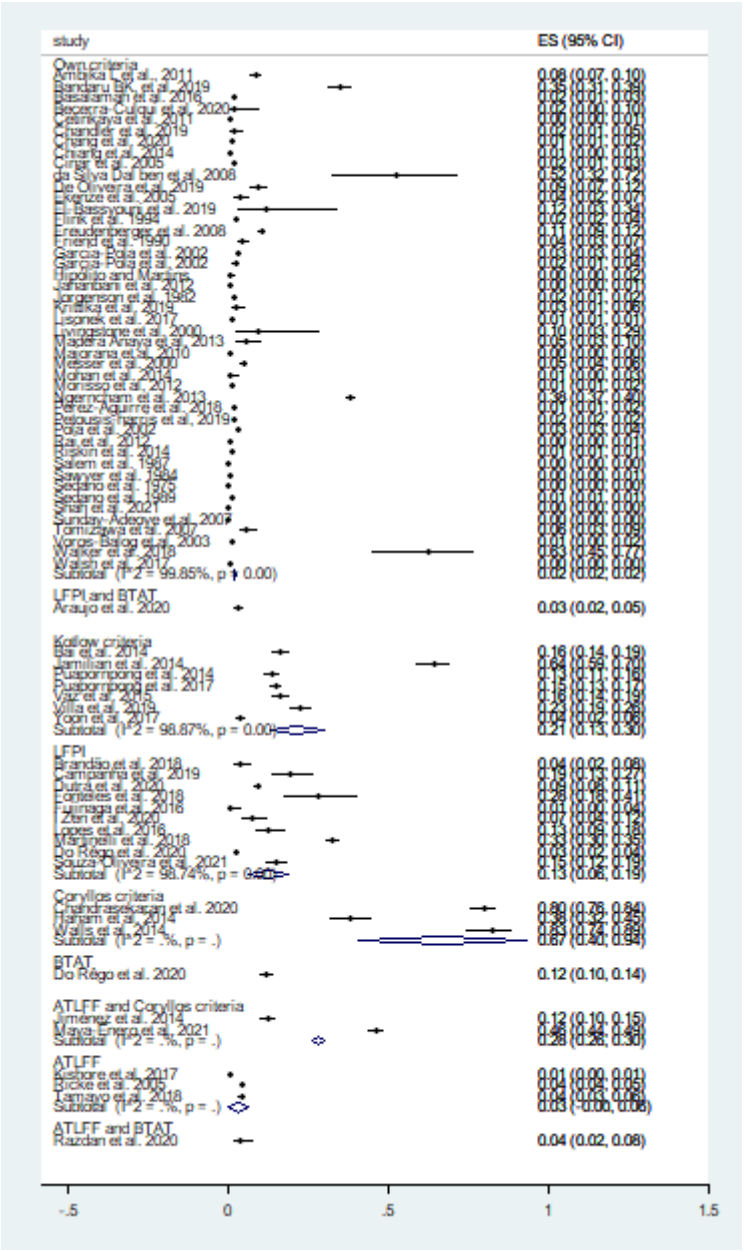
Diagnostic Criteria	Description
Assessment Tool for Lingual Frenulum Function (ATLFF)	The ATLFF was developed with the purpose of evaluating the function of the lingual frenulum, as well as the severity of ankylogossia in babies from zero to six months. The protocol consists of five items that assess the appearance of the tongue: “appearance of tongue when lifted”; “elasticity of frenulum”; “length of lingual frenulum when tongue lifted”; “attachment of lingual frenulum to tongue”; “attachment of lingual frenulum to inferior alveolar ridge”. Also, there are seven items that evaluate function: “lateralization”; “lift of tongue”; “extension of tongue”; “spread of anterior tongue”; cupping”; “peristalsis”; “snapback”. The result is established through scores, showing whether or not there is functional impairment (“perfect,” “acceptable,” or “function impaired.”), and consequently indicates the need to perform a frenotomy.
Bristol Tongue Assessment Tool (BTAT)	This tool allows the assessment of the lingual frenulum to be carried out in the maternity ward and consists of scores and classification of tongue functioning severity. Its main goal is to turn the assessment of the frenulum in neonates simple. Four elements are evaluated: “tongue tip appearance"; "attachment of frenulum to lower gum ridge" and "lift of tongue with mouth wide (during crying)"; "protrusion of tongue". All these items are scored and added together, with scores ranging from 0 to 8. Scores less than 3 indicate severe reduction in lingual function, demonstrating the possible need of frenotomy and the need of monitoring the procedure.
Coryllos criteria	According to the Coryllos criteria, ankyloglossya can be classified into four types, according to the distance between the tip of the tongue and the insertion of the lingual frenulum in: type 1 - attachment of the frenulum to the tip of the tongue; type 2 - two to four mm behind the tongue; type 3 - tongue- tie is the attachment to the mid-tongue and the middle of the floor of the mouth and type 4 is essentially against the base of the tongue. Types 1 and 2, considered "classic" akyloglossia, are the most common types, and incidence can up to 75%. Types 3 and 4 are less common and more difficult to diagnose, so they receive less treatment. Type 4 is more likely to cause difficulty in handling the bolus and dysphagia.

Lingual Frenulum Protocol for Infants (LFPI)	The LFPI is divided into three parts: clinical history; anatomical-functional evaluation and evaluation of non-nutritive sucking and nutritive sucking (for 5 minutes). The scores follow a scale of 0 to 3, in which 0 indicates free tongue movements; 1 indicates presence of any alteration, not necessarily due to the lingual frenulum; 2 indicates restriction of tongue movements; and 3 indicates the presence of alterations in the lingual frenulum and restriction of tongue movements. The three parts of this protocol have independent scores, so each part can be applied independently of one another until up to the 6th month of the baby's life. For neonatal screening, in the first 48 hours after delivery, only the anatomical and functional assessment of the baby is carried out for the diagnosis of ankyloglossia. At this stage, the protocol evaluates: 1) the positioning of the lip at rest; 2) tongue positioning during crying; 3) shape of the tip of the tongue when raised during crying or by the lifting maneuver; 4) thickness, fixation on the ventral sublingual surface of the tongue and fixation of the frenulum on the floor of the mouth. The sum of the questionnaire items refers to scores: 0-4 (normal), 5-6 (doubtful, and retest after 30 days) and 7 or more (altered). A score equal to or greater than 7 considers the need to release the lingual frenulum.
Kotlow criteria	The assessment is based on the length, in millimeters, of the tongue from the insertion of the lingual frenulum at its base to its tip. The severity of ankyloglossia is classified into: Class I: mild ankyloglossia - 12 to 16 mm; Class II: moderate ankyloglossia - 8 to 11 mm; Class III: severe ankyloglossia – 3 to 7 mm; Class IV: complete ankyloglossia – less than 3 mm. A tongue with normal mobility is when the length of the frenulum is greater than or equal to 16 mm. The other criteria for normal lingual mobility are: the tip of the tongue must be protruded without forming a crack in the tip; the tongue should reach the lower and upper lips without effort; there must be absence of ischemia at the lingual end during the retrusion movement; the tongue must not exert excessive forces on the lower incisors; the lingual frenulum cannot interfere with dentition or create a diastema between the mandibular central incisors; in babies, there should be no abrasion on the ventral side of the tongue, no interference with breastfeeding or speech difficulties associated with limited mobility

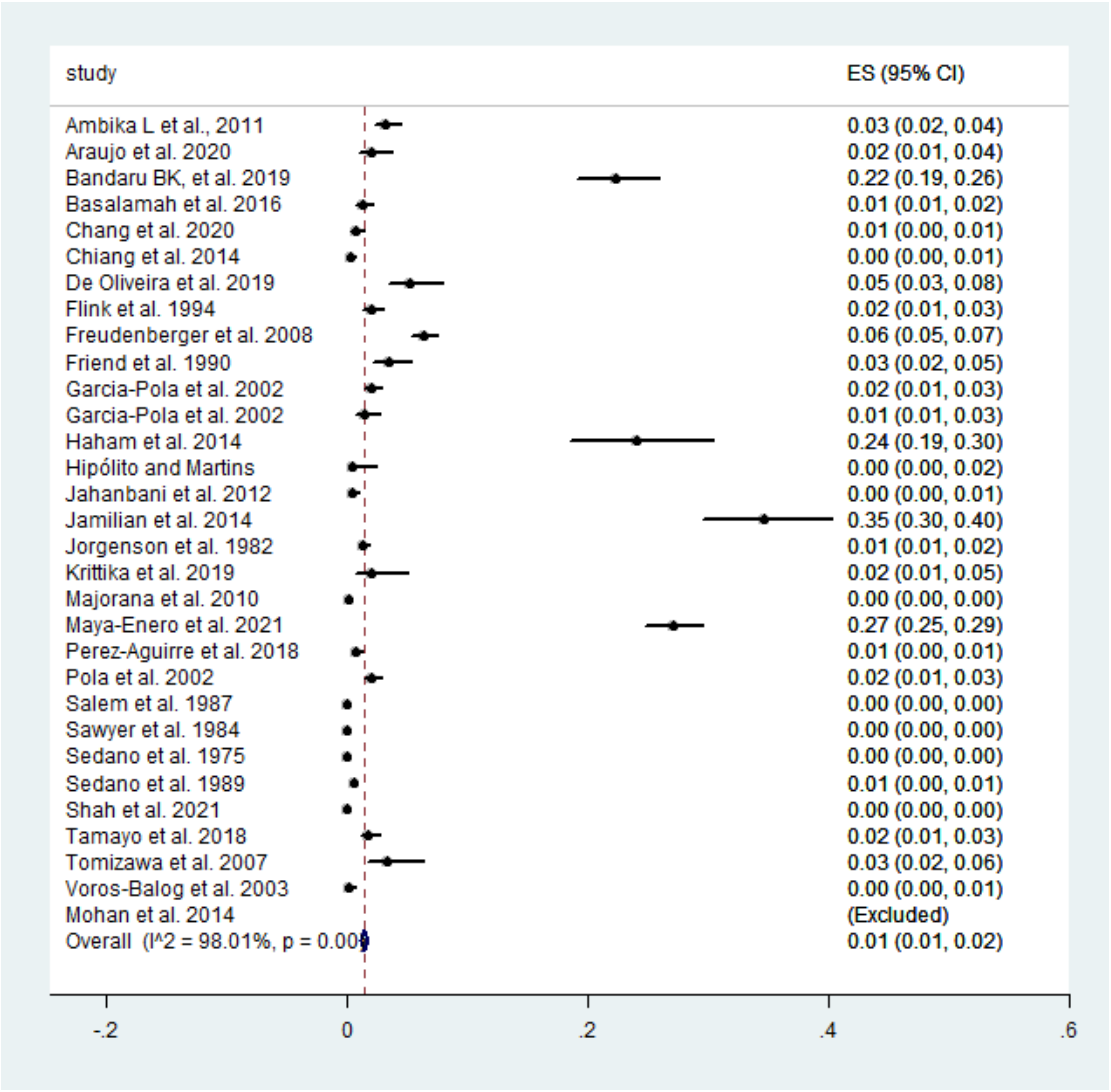
	of the tongue in children.



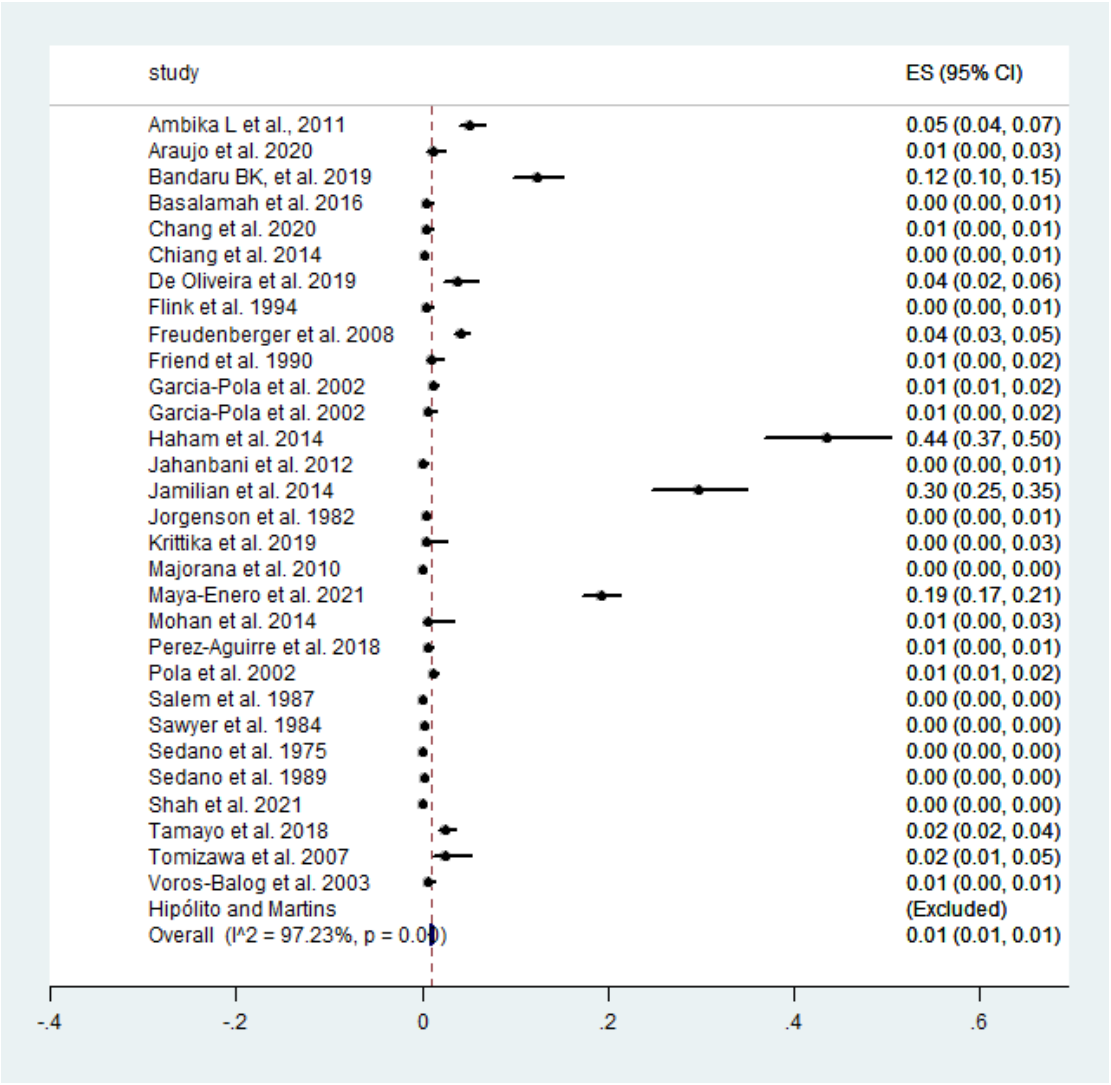
Appendix Figure 3: Random-effect meta-analysis of overall crude prevalence of ankyloglossia. Prevalence: ES (effect estimate).



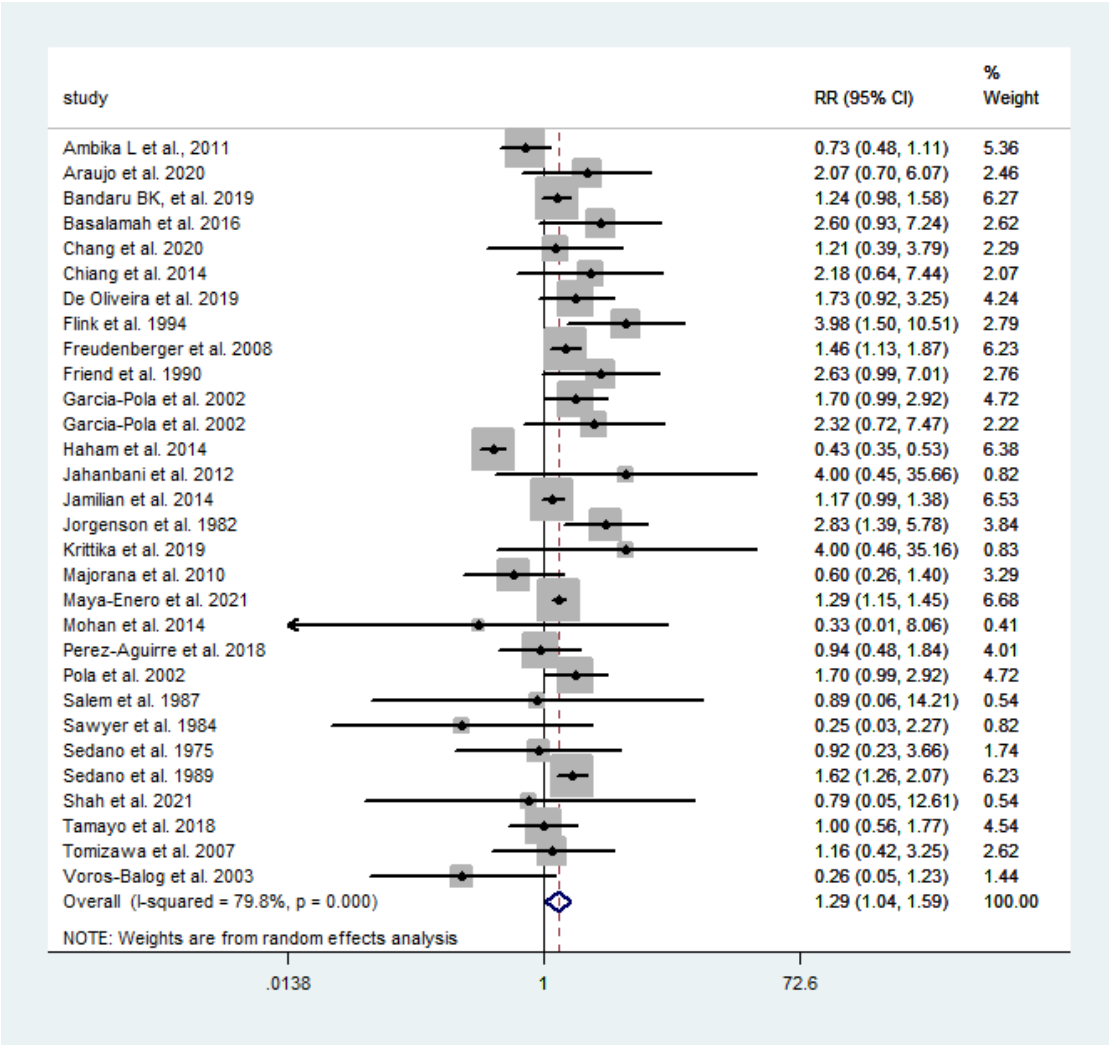
Appendix Figure 4: Mixed-effect meta-analysis of ankyloglossia subgrouped by diagnostic criteria. Prevalence: ES (effect estimate).



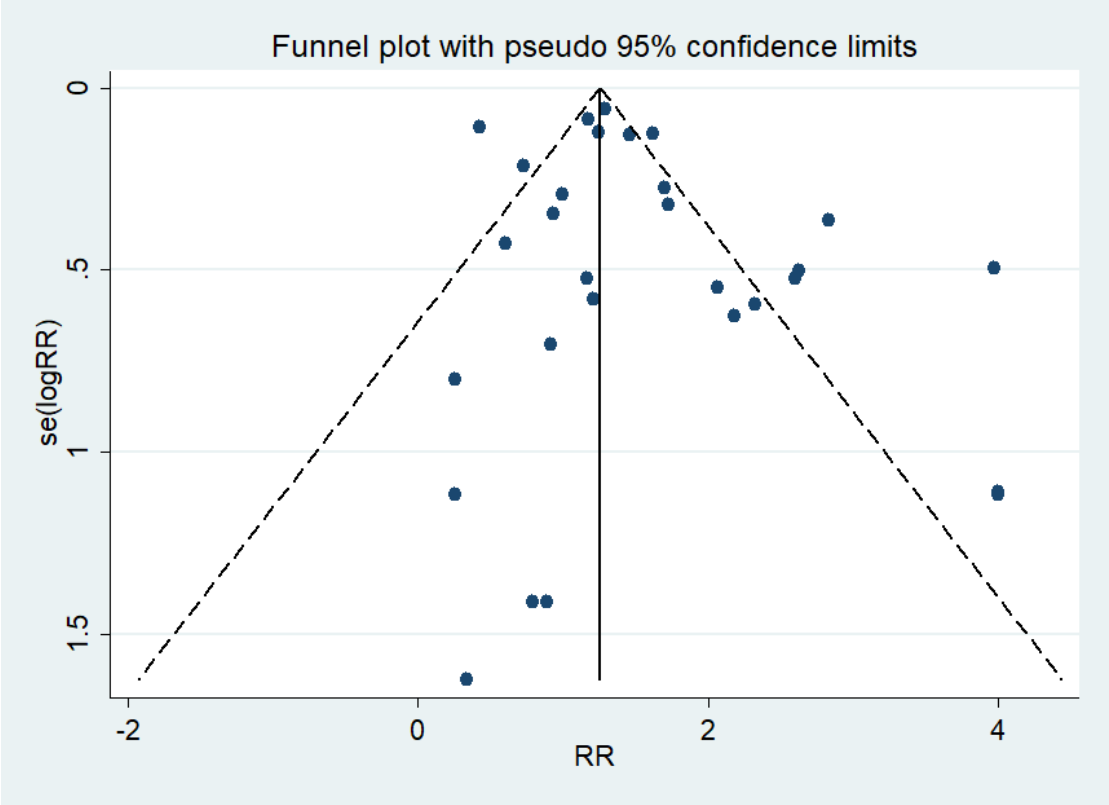
Appendix Figure 5: Random-effect meta-analysis of overall crude prevalence of ankyloglossia among boys. Prevalence: ES (effect estimate).



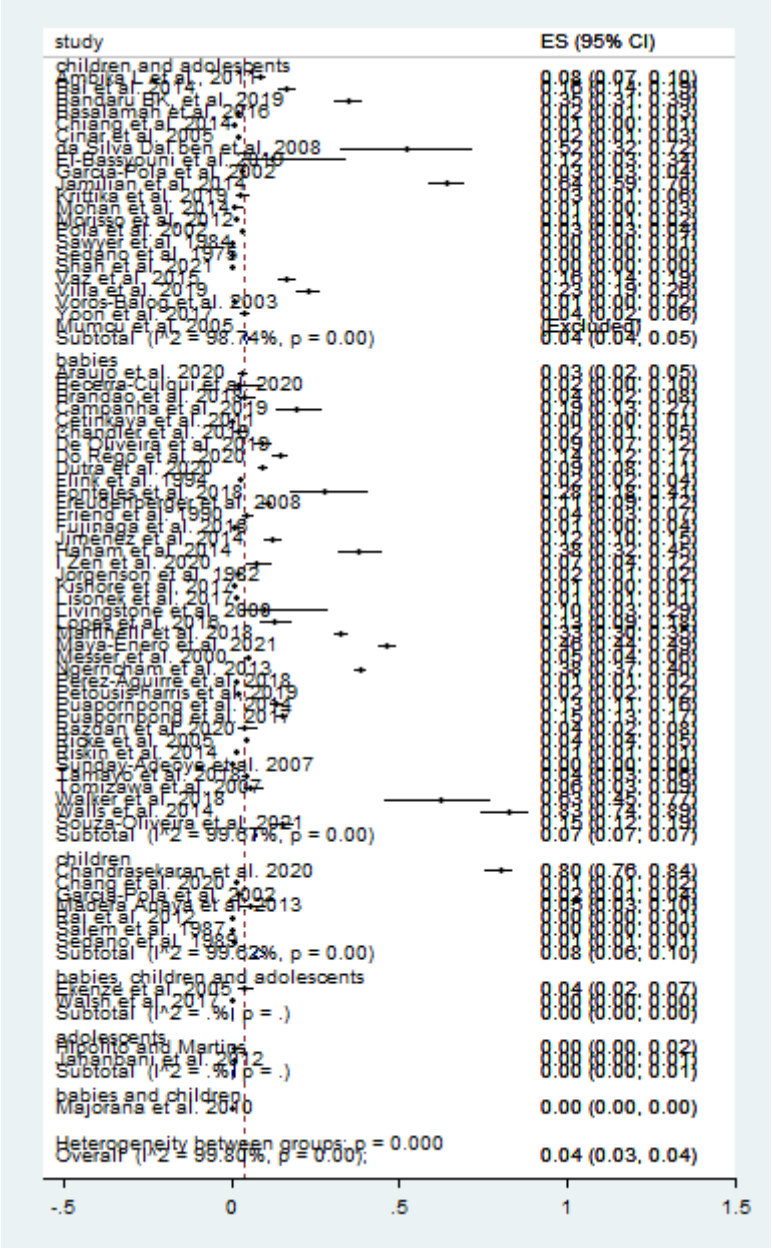
Appendix Figure 6: Random-effect meta-analysis of overall crude prevalence of ankyloglossia among girls. Prevalence: ES (effect estimate).



Appendix Figure 7: Random-effect meta-analysis comparing the occurrence of ankyloglossia between boys and girls. RR=PR (prevalence ratio).



Appendix Figure 8. Publication bias for effect estimate comparing boys and girls. Egger test: p= 0.091



Appendix Figure 9: Mixed-effect meta-analysis of prevalence of ankyloglossia subgrouped by age. Prevalence: ES (effect estimate).

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ANEXO A – Parecer de aprovação do projeto pelo Comitê de Ética em Pesquisa da UFMG

UNIVERSIDADE FEDERAL DE MINAS GERAIS
COMITÊ DE ÉTICA EM PESQUISA - COEP

Projeto: CAAE – 57295316.3.0000.5149

Interessado(a): Profa. Carolina C Martins
Departamento de Odontopediatria e Ortodontia
Faculdade de Odontologia- UFMG

DECISÃO

O Comitê de Ética em Pesquisa da UFMG – COEP aprovou, no dia 22 de agosto de 2016, a emenda abaixo relacionada, do projeto de pesquisa intitulado **"Lesões de mucosa em recém-nascidos"**.

- Atendimento de todas as recomendações do parecer consubstanciado.

O relatório final ou parcial deverá ser encaminhado ao COEP um ano após o início do projeto através da Plataforma Brasil.

Profa. Dra. Vivian Resende
Coordenadora do COEP-UFMG

Av. Pres. Antonio Carlos, 6627 – Unidade Administrativa II - 2º andar – Sala 2005 – Cep: 31270-901 – BH-MG
Telefax: (031) 3409-4592 - e-mail: coep@prpq.ufmg.br

ANEXO B – Parecer de aprovação do projeto pela Unidade Funcional Ginecologia, Obstetrícia e Neonatologia do Hospital das Clínicas – UFMG

Unidade Funcional Ginecologia, Obstetrícia e Neonatologia

A Unidade Funcional Ginecologia, Obstetrícia e Neonatologia têm como parecer favorável, à realização do Projeto de Pesquisa intitulado **"LESÕES DE MUCOSA EM RECÉM NASCIDOS"**, nesta Unidade Funcional.

Reiteramos que a sua realização será liberada por essa Unidade Funcional desde que não haja custos para Unidade Funcional da Ginecologia, Obstetrícia e Neonatologia.

Belo Horizonte, 23 de junho de 2.016.

Denise de Fátima Torres
Insc: 12129-0
Chefe UFG/ONeo - HC

Denise de Fátima Torres
Chefe da Unidade Ginecologia, Obstetrícia e Neonatologia.
Hospital das Clínicas - UFMG

Av. Alfredo Balena, 110/ 4º Andar - Stª1 Efigênia - BH – MG – CEP 30.- 130-100
Telefones: 3409-9421 Telefax: 3409-9996

ANEXO C – Critério de classificação econômica da Associação Brasileira de Empresas e Pesquisa (ABEP)

Critério Brasil 2015 e atualização da distribuição de classes para 2016

A metodologia de desenvolvimento do Critério Brasil que entrou em vigor no início de 2015 está descrita no livro *Estratificação Socioeconômica e Consumo no Brasil* dos professores Wagner Kamakura (Rice University) e José Afonso Mazzon (FEA /USP), baseado na Pesquisa de Orçamento Familiar (POF) do IBGE.

A regra operacional para classificação de domicílios, descrita a seguir, resulta da adaptação da metodologia apresentada no livro às condições operacionais da pesquisa de mercado no Brasil.

As organizações que utilizam o Critério Brasil podem relatar suas experiências ao Comitê do CCEB. Essas experiências serão valiosas para que o Critério Brasil seja permanentemente aprimorado.

A transformação operada atualmente no Critério Brasil foi possível graças a generosa contribuição e intensa participação dos seguintes profissionais nas atividades do comitê:

Luis Pilli (Coordenador) - LARC Pesquisa de Marketing
Bianca Ambrósio -TNS
Bruna Suzzara – IBOPE Inteligência
Marcelo Alves - Nielsen
Margareth Reis – GFK
Paula Yamakawa – IBOPE Inteligência
Renata Nunes - Data Folha
Sandra Mazzo - Ipsos
Tatiana Wakaguri – Kantar IBOPE Media

A ABEP, em nome de seus associados, registra o reconhecimento e agradece o envolvimento desses profissionais.

SISTEMA DE PONTOS

Variáveis

	Quantidade				
	0	1	2	3	4 ou +
Banheiros	0	3	7	10	14
Empregados domésticos	0	3	7	10	13
Automóveis	0	3	5	8	11
Microcomputador	0	3	6	8	11
Lava louca	0	3	6	6	6
Geladeira	0	2	3	5	5
Freezer	0	2	4	6	6
Lava roupa	0	2	4	6	6
DVD	0	1	3	4	6
Micro-ondas	0	2	4	4	4
Motocicleta	0	1	3	3	3
Secadora roupa	0	2	2	2	2

Grau de instrução do chefe de família e acesso a serviços públicos

Escolaridade da pessoa de referência	
Analfabeto / Fundamental I incompleto	0
Fundamental I completo / Fundamental II incompleto	1
Fundamental II completo / Médio incompleto	2
Médio completo / Superior incompleto	4
Superior completo	7

Serviços públicos		
	Não	Sim
Água encanada	0	4
Rua pavimentada	0	2

Distribuição das classes para 2016

As estimativas do tamanho dos estratos atualizados referem-se ao total Brasil e resultados das Macro Regiões, além do total das 9 Regiões Metropolitanas e resultados para cada uma das RM's (Porto Alegre, Curitiba, São Paulo, Rio de Janeiro, Belo Horizonte, Brasília, Salvador, Recife e Fortaleza).

As estimativas são baseadas em estudos probabilísticos do Datafolha, IBOPE Inteligência, GFK, IPSOS e Kantar IBOPE Media (LSE).

Classe	Brasil	Sudeste	Sul	Nordeste	Centro Oeste	Norte
A	2,9%	3,6%	3,4%	1,4%	4,2%	1,8%
B1	5,0%	6,2%	6,2%	2,7%	5,3%	3,4%
B2	17,3%	21,0%	20,6%	10,5%	18,7%	11,7%
C1	22,2%	25,3%	28,0%	15,1%	23,0%	17,9%
C2	25,6%	25,4%	24,8%	25,6%	27,5%	26,3%
D-E	27,0%	18,5%	17,0%	44,7%	21,3%	38,9%
TOTAL	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**

Classe	9RM's	POA	CWB	SP	RJ	BH	BSB	SSA	REC	FOR
A	4,3%	3,7%	5,4%	4,8%	3,5%	3,5%	9,9%	4,1%	2,0%	3,4%
B1	6,6%	6,5%	8,2%	7,5%	5,9%	5,7%	9,6%	5,2%	4,4%	4,3%
B2	19,5%	20,7%	24,3%	23,1%	17,5%	18,4%	22,0%	13,8%	13,2%	12,8%
C1	24,3%	27,0%	27,6%	28,4%	23,2%	24,0%	22,0%	18,1%	16,7%	15,0%
C2	25,9%	27,0%	22,8%	25,0%	26,6%	27,5%	21,7%	28,5%	28,5%	26,1%
D-E	19,4%	15,1%	11,7%	11,2%	23,3%	20,9%	14,8%	30,3%	35,2%	38,4%
TOTAL	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**

Cortes do Critério Brasil

Classe	Pontos
A	45 - 100
B1	38 - 44
B2	29 - 37
C1	23 - 28
C2	17 - 22
D-E	0 - 16

Estimativa para a Renda Média Domiciliar para os estratos do Critério Brasil

Abaixo são apresentadas as estimativas de renda domiciliar mensal para os estratos socioeconômicos. Os valores se baseiam na PNAD 2014 e representam aproximações dos valores que podem ser obtidos em amostras de pesquisas de mercado, mídia e opinião. A experiência mostra que a variância observada para as respostas à pergunta de renda é elevada, com sobreposições importantes nas rendas entre as classes. Isso significa que pergunta de renda não é um estimador eficiente de nível socioeconômico e não substitui ou complementa o questionário sugerido abaixo. O objetivo da divulgação dessas informações é oferecer uma ideia de característica dos estratos socioeconômicos resultantes da aplicação do Critério Brasil.

Estrato Sócio Economico	Renda média Domiciliar
A	20.888
B1	9.254
B2	4.852
C1	2.705
C2	1.625
D-E	768
TOTAL	3.130

PROCEDIMENTO NA COLETA DOS ITENS

É importante e necessário que o critério seja aplicado de forma uniforme e precisa. Para tanto, é fundamental atender integralmente as definições e procedimentos citados a seguir.

Para aparelhos domésticos em geral:

Devem ser considerados todos os bens que estão dentro do domicílio em funcionamento (incluindo os que estão guardados) independente da forma de aquisição: compra, empréstimo, aluguel, etc. Se o domicílio possui um bem que emprestou a outro, este não deve ser contado pois não está em seu domicílio atualmente. Caso não estejam funcionando, considere apenas se tiver intenção de consertar ou repor nos próximos seis meses.

Banheiro

O que define o banheiro é a existência de vaso sanitário. Considerar todos os banheiros e lavabos com vaso sanitário, incluindo os de empregada, os localizados fora de casa e os da(s) suíte(s). Para ser considerado, o banheiro tem que ser privativo do domicílio. Banheiros coletivos (que servem a mais de uma habitação) não devem ser considerados.

Empregados Domésticos

Considerar apenas os empregados mensalistas, isto é, aqueles que trabalham pelo menos cinco dias por semana, durmam ou não no emprego. Não esqueça de incluir babás, motoristas, cozinheiras, copeiras, arrumadeiras, considerando sempre os mensalistas.

Note bem: o termo empregado mensalista se refere aos empregados que trabalham no domicílio de forma permanente e/ou continua, pelo menos cinco dias por semana, e não ao regime de pagamento do salário.

Automóvel

Não considerar táxis, vans ou pick-ups usados para fretes, ou qualquer veículo usado para atividades profissionais. Veículos de uso misto (pessoal e profissional) não devem ser considerados.

Microcomputador

Considerar os computadores de mesa, laptops, notebooks e netbooks. Não considerar: calculadoras, agendas eletrônicas, tablets, palms, smartphones e outros aparelhos.

Lava-Louça

Considere a máquina com função de lavar as louças.

Geladeira e Freezer

No quadro de pontuação há duas linhas independentes para assinalar a posse de geladeira e freezer respectivamente. A pontuação será aplicada de forma independente:

Havendo uma geladeira no domicílio, serão atribuídos os pontos (2) correspondentes a posse de geladeira;
Se a geladeira tiver um freezer incorporado – 2ª porta – ou houver no domicílio um freezer independente serão atribuídos os pontos (2) correspondentes ao freezer. Dessa forma, esse domicílio totaliza 4 pontos na soma desses dois bens.

Lava-Roupa

Considerar máquina de lavar roupa, somente as máquinas automáticas e/ou semiautomática. O tanquinho NÃO deve ser considerado.

DVD

Considere como leitor de DVD (Disco Digital de Vídeo ou Disco Digital Versátil) o acessório doméstico capaz de reproduzir mídias no formato DVD ou outros formatos mais modernos, incluindo videogames, computadores, notebooks. Inclua os aparelhos portáteis e os acoplados em microcomputadores.
Não considere DVD de automóvel.

Micro-ondas

Considerar forno micro-ondas e aparelho com dupla função (de micro-ondas e forno elétrico).

Motocicleta

Não considerar motocicletas usadas exclusivamente para atividades profissionais. Motocicletas apenas para uso pessoal e de uso misto (pessoal e profissional) devem ser consideradas.

Secadora de roupas

Considerar a máquina de secar roupa. Existem máquinas que fazem duas funções, lavar e secar. Nesses casos, devemos considerar esse equipamento como uma máquina de lavar e como uma secadora.

Modelo de Questionário sugerido para aplicação

P.XX Agora vou fazer algumas perguntas sobre itens do domicilio para efeito de classificação econômica. Todos os itens de eletroeletrônicos que vou citar devem estar funcionando, incluindo os que estão guardados. Caso não estejam funcionando, considere apenas se tiver intenção de consertar ou repor nos próximos seis meses.

INSTRUÇÃO: Todos os itens devem ser perguntados pelo entrevistador e respondidos pelo entrevistado.
Vamos começar? No domicílio tem_____ (LEIA CADA ITEM)

		QUANTIDADE QUE POSSUI			
ITENS DE CONFORTO	NÃO POSSUI	1	2	3	4+
Quantidade de automóveis de passeio exclusivamente para uso particular					
Quantidade de empregados mensalistas, considerando apenas os que trabalham pelo menos cinco dias por semana					
Quantidade de máquinas de lavar roupa, excluindo tanquinho					
Quantidade de banheiros					
DVD, incluindo qualquer dispositivo que leia DVD e desconsiderando DVD de automóvel					
Quantidade de geladeiras					
Quantidade de *freezers* independentes ou parte da geladeira duplex					
Quantidade de microcomputadores, considerando computadores de mesa, laptops, notebooks e netbooks e desconsiderando tablets, palms ou smartphones					
Quantidade de lavadora de louças					
Quantidade de fornos de micro-ondas					
Quantidade de motocicletas, desconsiderando as usadas exclusivamente para uso profissional					
Quantidade de máquinas secadoras de roupas, considerando lava e seca					

A água utilizada neste domicílio é proveniente de?	
1	Rede geral de distribuição
2	Poço ou nascente
3	Outro meio

Considerando o trecho da rua do seu domicílio, você diria que a rua é:	
1	Asfaltada/Pavimentada
2	Terra/Cascalho

Qual é o grau de instrução do chefe da família? Considere como chefe da família a pessoa que contribui com a maior parte da renda do domicílio.

Nomenclatura atual	Nomenclatura anterior
Analfabeto / Fundamental I incompleto	Analfabeto/Primário Incompleto
Fundamental I completo / Fundamental II incompleto	Primário Completo/Ginásio Incompleto
Fundamental completo/Médio incompleto	Ginásio Completo/Colegial Incompleto
Médio completo/Superior incompleto	Colegial Completo/Superior Incompleto
Superior completo	Superior Completo

OBSERVAÇÕES IMPORTANTES

Este critério foi construído para definir grandes classes que atendam às necessidades de segmentação (por poder aquisitivo) da grande maioria das empresas. Não pode, entretanto, como qualquer outro critério, satisfazer todos os usuários em todas as circunstâncias. Certamente há muitos casos em que o universo a ser pesquisado é de pessoas, digamos, com renda pessoal mensal acima de US$ 30.000. Em casos como esse, o pesquisador deve procurar outros critérios de seleção que não o CCEB.

A outra observação é que o CCEB, como os seus antecessores, foi construído com a utilização de técnicas estatísticas que, como se sabe, sempre se baseiam em coletivos. Em uma determinada amostra, de determinado tamanho, temos uma determinada probabilidade de classificação correta, (que, esperamos, seja alta) e uma probabilidade de erro de classificação (que, esperamos, seja baixa).

Nenhum critério estatístico, entretanto, tem validade sob uma análise individual. Afirmações frequentes do tipo *"... conheço um sujeito que é obviamente classe D, mas pelo critério é classe B..."* não invalidam o critério que é feito para funcionar estatisticamente. Servem, porém, para nos alertar, quando trabalhamos na análise individual, ou quase individual, de comportamentos e atitudes (entrevistas em profundidade e discussões em grupo respectivamente). Numa discussão em grupo um único caso de má classificação pode pôr a perder todo o grupo. No caso de entrevista em profundidade os prejuízos são ainda mais óbvios. Além disso, numa pesquisa qualitativa, raramente uma definição de classe exclusivamente econômica será satisfatória.

Portanto, é de fundamental importância que todo o mercado tenha ciência de que o CCEB, ou qualquer outro critério econômico, não é suficiente para uma boa classificação em pesquisas qualitativas. Nesses casos deve-se obter além do CCEB, o máximo de informações (possível, viável, razoável) sobre os respondentes, incluindo então seus comportamentos de compra, preferências e interesses, lazer e hobbies e até características de personalidade.

Uma comprovação adicional da adequação do Critério de Classificação Econômica Brasil é sua discriminação efetiva do poder de compra entre as diversas regiões brasileiras, revelando importantes diferenças entre elas.

ANEXO D – Normas para submissão de manuscrito no periódico *International Journal of Paediatric Dentistry*

Disponível em:

https://onlinelibrary.wiley.com/page/journal/1365263x/homepage/forauthors.html

- **Author Guidelines**

1. SUBMISSION

Authors should kindly note that submission implies that the content has not been published or submitted for publication elsewhere except as a brief abstract in the proceedings of a scientific meeting or symposium.

Once the submission materials have been prepared in accordance with the Author Guidelines, manuscripts should be submitted online at https://mc.manuscriptcentral.com/ijpd.

Data protection

By submitting a manuscript to or reviewing for this publication, your name, email address, and affiliation, and other contact details the publication might require, will be used for the regular operations of the publication, including, when necessary, sharing with the publisher (Wiley) and partners for production and publication. The publication and the publisher recognize the importance of protecting the personal information collected from users in the operation of these services, and have practices in place to ensure that steps are taken to maintain the security, integrity, and privacy of the personal data collected and processed. You can learn more at **https://authorservices.wiley.com/statements/data-protection-policy.html**.

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Please find the Wiley preprint policy here.

This journal accepts articles previously published on preprint servers.

International Journal of Paediatric Dentistry will consider for review articles previously available as preprints. Authors may also post the submitted version of a manuscript to a preprint server at any time. Authors are requested to update any pre-publication versions with a link to the final published article.

For help with submissions, please contact: **IJPDedoffice@wiley.com**

2. AIMS AND SCOPE

International Journal of Paediatric Dentistry publishes papers on all aspects of paediatric dentistry including: growth and development, behaviour management, diagnosis, prevention, restorative treatment and issue relating to medically compromised children or those with disabilities. This peer-reviewed journal features scientific articles, reviews, case reports, short communications and abstracts of current paediatric dental research. Analytical studies with a scientific novelty value are preferred to descriptive studies. Case reports illustrating unusual conditions and clinically relevant observations are

acceptable but must be of sufficiently high quality to be considered for publication; particularly the illustrative material must be of the highest quality.

3. MANUSCRIPT CATEGORIES AND REQUIREMENTS

i. Original Articles

Divided into: Summary, Introduction, Material and methods, Results, Discussion, Bullet points, Acknowledgements, References, Figure legends, Tables and Figures arranged in this order.

- **Summary** should be structured using the following subheadings: Background, Hypothesis or Aim, Design, Results, and Conclusions and should be less than 200 words.
- **Introduction** should be brief and end with a statement of the aim of the study or hypotheses tested. Describe and cite only the most relevant earlier studies. Avoid presentation of an extensive review of the field.
- **Material and methods** should be clearly described and provide enough detail so that the observations can be critically evaluated and, if necessary repeated. Use section subheadings in a logical order to title each category or method. Use this order also in the results section. Authors should have considered the ethical aspects of their research and should ensure that the project was approved by an appropriate ethical committee, which should be stated. Type of statistical analysis must be described clearly and carefully.
- **Results** should clearly and concisely report the findings, and division using subheadings is encouraged. Double documentation of data in text, tables or figures is not acceptable. Tables and figures should not include data that can be given in the text in one or two sentences.
- **Discussion** section presents the interpretation of the findings. This is the only proper section for subjective comments and reference to previous literature. Avoid repetition of results, do not use subheadings or reference to tables in the results section.
- **Bullet Points:** Authors will need to provide no more than 3 ‘key points’ that summarise the key messages of their paper to be published with their article. The key points should be written with a practitioner audience in mind under the heading: *Why this paper is important to paediatric dentists.

References: Maximum 30.

ii. Review Articles

May be invited by the Editor.

iii. Systematic reviews

We consider publishing systematic reviews if the manuscript has comprehensive and unbiased sampling of literature and covering topics related to Paediatric Dentistry.

References: Maximum 30.

Articles for the *International Journal of Paediatric Dentistry* should include: a) description of search strategy of relevant literature (search terms and databases), b) inclusion criteria (language, type of studies i.e. randomized controlled trial or other, duration of studies and chosen endpoints, c) evaluation of papers and level of evidence. For examples see:

Twetman S, Axelsson S, Dahlgren H et al. Caries-preventive effect of fluoride toothpaste: a systematic review. Acta Odontologica Scandivica 2003; 61: 347-355.

Paulsson L, Bondemark L, Söderfeldt B. A systematic review of the consequences of premature birth on palatal morphology, dental occlusion, tooth-crown dimensions, and tooth maturity and eruption. Angle Orthodontist 2004; 74: 269-279.

iv. Short Communications

Brief scientific articles or short case reports may be submitted, which should be no longer than three pages of double-spaced text and include a maximum of three illustrations. They should contain important, new, definitive information of sufficient significance to warrant publication. They should not be divided into different parts and summaries are not required.

References: Maximum 30.

v. Brief Clinical Reports/Case Reports

Short papers not exceeding 800 words, including a maximum of three illustrations and five references may be accepted for publication if they serve to promote communication between clinicians and researchers. If the paper describes a genetic disorder, the OMIM unique six-digit number should be provided for online cross reference (Online Mendelian Inheritance in Man).

A paper submitted as a Brief Clinical/Case Report should include the following:

- a short **Introduction** (avoid lengthy reviews of literature);
- the **Case report** itself (a brief description of the patient/s, presenting condition, any special investigations and outcomes);
- a **Discussion** which should highlight specific aspects of the case(s), explain/interpret the main findings and provide a scientific appraisal of any previously reported work in the field.
- **Bullet Points:** Authors will need to provide no more than 3 'key points' that summarise the key messages of their paper to be published with their article. The key points should be written with a practitioner audience in mind under the heading: *Why this paper is important to paediatric dentists.

vi. Letters to the Editor

Should be sent directly to the editor for consideration in the journal.

4. PREPARING THE SUBMISSION

Cover Letters

Cover letters are not mandatory; however, they may be supplied at the author's discretion.

Parts of the Manuscript

The manuscript should be submitted in separate files: title page; main text file; figures.

Title page

The title page should contain:
i. A short informative title that contains the major key words. The title should not contain abbreviations (see Wiley's **best practice SEO tips**);
ii. A short running title of less than 50 characters;
iii. The full names of the authors and a statement of author contributions, e.g. Author contributions: A.S. and K.J. conceived the ideas; K.J. and R.L.M. collected the data; R.L.M. and P.A.K. analysed the data; and A.S. and K.J. led the writing;
iv. The author's institutional affiliations where the work was conducted, with a footnote for the author's present address if different from where the work was conducted;
v. Acknowledgments;
vi. Word count (excluding tables)

Authorship

Please refer to the journal's authorship policy the Editorial Policies and Ethical Considerations section for details on eligibility for author listing.

Acknowledgments

Contributions from anyone who does not meet the criteria for authorship should be listed, with permission from the contributor, in an Acknowledgments section. Financial and material support should also be mentioned. Thanks to anonymous reviewers are not appropriate.

Conflict of Interest Statement

Authors will be asked to provide a conflict of interest statement during the submission process. For details on what to include in this section, see the section 'Conflict of Interest' in the Editorial Policies and Ethical Considerations section below. Submitting authors should ensure they liaise with all co-authors to confirm agreement with the final statement.

Main Text File

As papers are double-blind peer reviewed the main text file should not include any information that might identify the authors.

The main text file should be presented in the following order:

i. Title, abstract and key words;
ii. Main text;
iii. References;
iv. Tables (each table complete with title and footnotes);
v. Figure legends;
vi. Appendices (if relevant).

Figures and supporting information should be supplied as separate files.

Abstract

Abstracts and keywords are required for some manuscript types. For details on manuscript types that require abstracts, please refer to the 'Manuscript Types and Criteria' section.

Keywords

Please provide 3-6 keywords. Keywords should be taken from the list provided at submission in ScholarOne.

Main Text

- As papers are double-blind peer reviewed, the main text file should not include any information that might identify the authors.
- The journal uses British spelling; however, authors may submit using either option, as spelling of accepted papers is converted during the production process.

References

All references should be numbered consecutively in order of appearance and should be as complete as possible. In text citations should cite references in consecutive order using Arabic superscript numerals. For more information about AMA reference style please consult the **AMA Manual of Style**

Sample references follow:

Journal article

1. King VM, Armstrong DM, Apps R, Trott JR. Numerical aspects of pontine, lateral reticular, and

inferior olivary projections to two paravermal cortical zones of the cat cerebellum. J Comp Neurol 1998;390:537-551.

Book
2. Voet D, Voet JG. Biochemistry. New York: John Wiley & Sons; 1990. 1223 p.

Internet document
3. American Cancer Society. Cancer Facts & Figures 2003. http://www.cancer.org/downloads/STT/CAFF2003PWSecured.pdf Accessed March 3, 2003

Tables

Tables should be self-contained and complement, not duplicate, information contained in the text. They should be supplied as editable files, not pasted as images. Legends should be concise but comprehensive – the table, legend, and footnotes must be understandable without reference to the text. All abbreviations must be defined in footnotes. Footnote symbols: †, ‡, §, ¶, should be used (in that order) and *, **, *** should be reserved for P-values. Statistical measures such as SD or SEM should be identified in the headings.

Figure Legends

Legends should be concise but comprehensive – the figure and its legend must be understandable without reference to the text. Include definitions of any symbols used and define/explain all abbreviations and units of measurement.

Figures

Although authors are encouraged to send the highest-quality figures possible, for peer-review purposes, a wide variety of formats, sizes, and resolutions are accepted.

In the text, please reference figures as for instance 'Figure 1', 'Figure 2' to match the tag name you choose for the individual figure files uploaded.

Colour Figures. Figures submitted in colour may be reproduced in colour online free of charge. Please note, however, that it is preferable that line figures (e.g. graphs and charts) are supplied in black and white so that they are legible if printed by a reader in black and white.

Data Citation

Please review Wiley's data citation policy here.

Additional Files

Appendices

Appendices will be published after the references. For submission they should be supplied as separate files but referred to in the text.

Supporting Information

Supporting information is information that is not essential to the article, but provides greater depth and background. It is hosted online and appears without editing or typesetting. It may include tables, figures, videos, datasets, etc.

Note: if data, scripts, or other artefacts used to generate the analyses presented in the paper are available via a publicly available data repository, authors should include a reference to the location of the material within their paper.

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Revised manuscripts must be uploaded within 2 months of authors being notified of conditional acceptance pending satisfactory revision. Locate your manuscript under 'Manuscripts with Decisions' and click on 'Submit a Revision' to submit your revised manuscript. Please remember to delete any old files uploaded when you upload your revised manuscript. All revisions must be accompanied by a cover letter to the editor. The letter must a) detail on a point-by-point basis the author's response to each of the referee's comments, and b) a revised manuscript highlighting exactly what has been changed in the manuscript after revision.

Resource Identification Initiative

The journal supports the **Resource Identification Initiative**, which aims to promote research resource identification, discovery, and reuse. This initiative, led by the **Neuroscience Information Framework** and the **Oregon Health & Science University Library**, provides unique identifiers for antibodies, model organisms, cell lines, and tools including software and databases. These IDs, called Research Resource Identifiers (RRIDs), are machine-readable and can be used to search for all papers where a particular resource was used and to increase access to critical data to help researchers identify suitable reagents and tools.

Authors are asked to use RRIDs to cite the resources used in their research where applicable in the text, similar to a regular citation or Genbank Accession number. For antibodies, authors should include in the citation the vendor, catalogue number, and RRID both in the text upon first mention in the Methods section. For software tools and databases, please provide the name of the resource followed by the resource website, if available, and the RRID. For model organisms, the RRID alone is sufficient.

Additionally, authors must include the RRIDs in the list of keywords associated with the manuscript.

To Obtain Research Resource Identifiers (RRIDs)

1. Use the Resource Identification Portal, created by the Resource Identification Initiative Working Group.
2. Search for the research resource (please see the section titled “Search Features and Tips” for more information).
3. Click on the “Cite This” button to obtain the citation and insert the citation into the manuscript text.

If there is a resource that is not found within the **Resource Identification Portal**, authors are asked to register the resource with the appropriate resource authority. Information on how to do this is provided in the “Resource Citation Guidelines” section of the Portal.

If any difficulties in obtaining identifiers arise, please contact **rii-help@scicrunch.org** for assistance.

Example Citations

Antibodies: "Wnt3 was localized using a rabbit polyclonal antibody C64F2 against Wnt3 (Cell Signaling Technology, Cat# 2721S, RRID: AB_2215411)"

Model Organisms: "Experiments were conducted in c. elegans strain SP304 (RRID:CGC_SP304)"

Cell lines: "Experiments were conducted in PC12 CLS cells (CLS Cat# 500311/p701_PC-12, RRID:CVCL_0481)"

Tools, Software, and Databases: "Image analysis was conducted with CellProfiler Image Analysis Software, V2.0 (http://www.cellprofiler.org, RRID:nif-0000-00280)"

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ANEXO E – Artigo puplicado no periódico *Journal of Clinical Neonatology*

Original Article

Oral Mucosal Lesions in Newborns: Relationship with Prematurity, Low Birth Weight, and Associated Factors

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ABSTRACT

Background: An increase in prematurity and low birth weight (LBW) has been observed worldwide, to which several factors may be associated. This cross-sectional study aimed to evaluate the relationship between gestational age and LBW with oral mucosal lesions in newborns, maternal health conditions, newborn health conditions, and socioeconomic levels. **Materials and Methods:** The sample was comprised of 431 pairs of mothers-newborns born from a high and medium complexity hospital (CAAE nº: 57295316.3.0000.5149). Maternal health conditions and childbirth information were collected through the medical records and mothers answered a questionnaire on socioeconomic indicators. Oral mucosal lesions were evaluated by oral clinical examination. Gestational age and birth weight were analyzed, together with oral mucosal lesions and related factors, through bivariate and multivariate logistic regression models (α = 5%). **Results:** Prematurity and LBW were associated with Epstein pearls (odds ratio [OR]: 1.7; 95% confidence interval [CI]: 1.03–3.0; OR: 1.8; 95% CI: 1.1–3.2, respectively) and mucocele (OR: 4.6; 95% CI: 1.3–16.1; OR: 3.7; 95% CI: 1.1–13.1, respectively), but not ankyloglossia (OR: 1.0; 95% CI: 0.5–2.1; OR: 0.7; 95% CI: 0.3–1.6, respectively) or breastfeeding (OR: 0.5; 95% CI: 0.1-2.1; OR: 1.9; 95% IC: 0.2–15.6, respectively). **Conclusion:** Preterm and LBW newborns were more likely to have Epstein pearls and mucocele than full terms. Breastfeeding and ankyloglossia were not associated with prematurity and LBW.

Keywords: *Low birth weight, newborn, oral mucosal lesion, oral pathology, preterm birth*

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Introduction

Premature infants are those born with a gestational age of 36 weeks and 6 days or less. Low birth weight (LBW) is defined as a newborn with <2500 g.[1,2] These conditions may have short and long-term consequences on neonatal health.[3,4] The care offered throughout the gestational and postnatal period, for both mother and newborn, must consist of early identification of possible health risk factors.[5] Preterm birth can affect craniofacial complex structures,[6,7] since the shorter the gestational age at birth, the greater the risk of congenital changes.[8] Thus, oral clinical alterations in newborns are very common, such as inclusion cysts, mucocele, and ankyloglossia.[6-9]

The inclusion cysts are classified according to their location: (1) Epstein pearls occur in the region of the mean palatine raphe, (2) Bohn's nodules occur on the buccal or lingual surfaces of the alveolar ridge, and (3) dental lamina cysts occur bilaterally on the maxillary or mandibular alveolar ridge.[10] Most of these alterations are rarely observed after the first month of life due to their inoculum and/or transitory character.[11] However, there are cases in which these cysts occur more

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severely, leading to the occurrence of secondary lesions in the oral mucosa, causing pain and difficulties during breastfeeding,[12] and consequently to early weaning.

Mucocele is a benign oral lesion commonly found in newborns and may be caused by mechanical trauma, resulting in the rupture of the secretory ducts of the salivary glands, which leads to the formation of a cystic cavity filled with mucus. Mucoceles can be found on the lips and cheeks, as well as on the floor of the mouth.[13]

Ankyloglossia is characterized when there is a shortening or thickening of the lingual frenulum. These characteristics can lead to a decrease in the free lingual portion, which in turn causes functional restriction, which may interfere with speech, in the position of the dental arches and teeth, although it does not seem to affect breastfeeding.[14-16]

Although oral mucosal lesions have been discussed previously, most studies are only descriptive.[10,11,12] Two studies evaluated the relationship between inclusion cysts and prematurity and LBW.[9,17] However, other types of oral mucosal lesions other than inclusion cysts were not analyzed. It is important that health professionals closely monitor pregnant women and the fetus during pregnancy, at all levels of complexity, to maintain the health of the newborn. Therefore, it is necessary to identify possible oral changes that may be associated with the general health condition of newborns and that may influence early weaning. Thus, our study aimed to evaluate the relationship between gestational age and LBW with oral mucosal lesions in newborns and associated factors.

Materials and Methods

This cross-sectional study was conducted at a University Hospital, a reference center in care for pregnant women under gestational risk, located in Belo Horizonte, Brazil. Data were collected from August 2016 to April 2017, and the study was approved by the Human Research Ethics Committee of the Federal University of Minas Gerais (CAAE # 57295316.3.00005149). The inclusion criteria were: all mothers who were hospitalized at the time of data collection and their newborns of both sexes. The exclusion criteria were newborns with neurological disabilities, craniofacial anomalies, and heart disease at birth reported on the medical records. Those mothers who agreed to participate signed an informed consent form.

The sample size was calculated using a prevalence of 56.4% of oral mucosal lesions,[18] with a margin of error of 5% and a 95% confidence interval (CI). A minimum sample of 378 newborns was determined, and 20% were added to compensate for possible losses, generating an estimated final sample of 453 newborns.

A theoretical training exercise was performed through pictures of oral mucosal lesions, followed by an oral clinical examination in newborns who did not participate in the main study. Calibration was conducted by a gold standard, expert in pediatric dentistry. The kappa value was 0.90 for inter-examiner agreement between the examiner and the gold standard.

A pilot study was conducted with 10 pairs of mothers/newborns before the main study. Participants were selected at the same hospital where the main study was conducted. As there were no intercurrences at this stage and no changes were necessary, all participants were included in the main study. The questionnaire and clinical examinationss were adequate.

Oral mucosal lesions were clinically diagnosed by the calibrated examiner. The newborns were lying down in their hospital crib and the examiner used a sterile clinical mirror, cotton swab, and artificial headlight. A research assistant took notes during oral examinations. The research team used appropriate personal protective equipment. The evaluated oral mucosal lesions included: Epstein Pearls, dental lamina cysts, Bohn's nodules, ankyloglossia, and mucocele, as described elsewhere.[9]

Through newborn's medical records, we collected the following data: newborn's sex, gestational age, birth weight, presence of infections (parasitic and viral infectious diseases, such as candidiasis, syphilis, human immunodeficiency virus [HIV] and infections caused by maternal urinary tract infection), need to be in the incubator, and admission to a neonatal intensive care unit (NICU) before being examined at the rooming-in.

The mothers were approached by the researchers in their hospital beds in the Rooming-in and filled a structured questionnaire with information on gestational habits, use of medications during pregnancy, history of previous diseases, and socioeconomic level (defined according to the monthly family income and the Brazilian minimum wage[19]).

Data were also collected related to mothers through medical records: sexually transmitted infections (HIV, Syphilis), previous health changes (parasitic and viral infectious diseases, cancers, Diabetes Mellitus), type of childbirth (vaginal childbirth, cesarean birth), and high-risk pregnancy. High-risk pregnancy was collected through the medical records, defined by complications developed during pregnancy or pre-existing comorbidities during pregnancy.[6] The following conditions were considered high-risk pregnancy:

diabetes mellitus, infectious diseases (HIV, Syphilis), anemia, hypertensive disorders (chronic hypertension, eclampsia, pre-eclampsia), cardiovascular disease, respiratory diseases, and changes in amniotic fluid volume (polyhydramnios/oligohydramnios).

The main variables were categorized as: birth weight (≥2500g; <2500g) and gestational age (full-term: ≥37 weeks; preterm: <37 weeks).

The other variables were categorized as type of childbirth (vaginal childbirth/cesarean section), newborn sex (female/male), mother's age (up to 19 years; 20 to 35 years; 36 years and over), and socioeconomic level. The socioeconomic level was categorized as "high" and "low" according to the questionnaire of the standard criterion of economic classification of the Brazilian Association of Research Companies, as described elsewhere.[19] The other variables were dichotomized into "yes" for the presence of the condition and "no" for the absence of the condition.

Data were entered into the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY, USA: IBM Corp.).

Data analysis included descriptive statistics (frequency distribution, mean, and standard deviation). Bivariate and multivariate logistic regression analyses were conducted to verify the association between preterm birth or birth weight and other variables. The quality of models was tested by the Hosmer–Lemeshow test. Model #1 (bivariate analysis), which included all variables, was not adjusted. Model #2 included all the independent variables with $P < 0.20$. For Model #3, we looked for a better fit model than Model #2, when appropriate.

Results

The final sample was comprised of 431 pairs of mothers/newborns. The response rate was 95% and only 5.0% of the sample was excluded from the study due to incorrect completion of the questionnaire. Seventy-three newborns (16.9%) were preterms and 69 (16%) were LBW. The mean maternal age was 27.3 years ± 7.12 (minimum = 15; maximum = 59 years). Of the total of newborns, 54.1% were males, with an average of 3.0 ± 3.4 days of life.

The minimum weight at birth was 1.690 kg and the maximum weight was 4.700 kg (mean = 3.056 kg ± 531.26 g). The minimum preterm birth was 33 weeks and the maximum full-term birth was 42 weeks (mean = 38.2 weeks ± 1.83).

Table 1 shows bivariate (Model #1) and multivariate (Models #2 and #3) analyses for comparison between preterm and full-term birth. Data for gestational age were missing on 13 of the medical records, and 418 newborns were included in this analysis. Model #1 showed that babies who were not breastfed (odds ratio [OR]: 0.5; 95% CI: 0.1–2.1) and who presented ankyloglossia (OR: 1.0; 95% CI: 0.5–2.1) were not associated with prematurity. NICU and incubator were collinear variables ($P < 0.001$), and NICU was removed from the final adjusted multivariate model (Model #3). The type of birth and previous health change was also removed for a better adjustment of the model (Hosmer and Lemeshow test- $P = 0.708$). Model #3 showed that newborns that had Epstein pearls had a 1.7-fold greater chance (OR: 1.7; 95% CI: 1.03—3.0) of belonging to the preterm group than did those without Epstein pearls. Newborns who presented mucocele had a 4.6-fold greater chance (OR: 4.6; 95% CI: 1.3–16.1) of belonging to the preterm group than those without mucocele. Also associated with high-risk pregnancy were prematurity (OR: 2.3; 95% CI: 1.3–3.9), being in the incubator (OR: 3.2; 95% CI: 1.7–5.9), and low socioeconomic status (OR: 2.4; 95% CI: 1.1–5.2).

Table 2 shows bivariate (Model #1) and multivariate (Models #2) analyses for birth weight. There were six missing pieces of data for birth weight on the medical records, and 425 newborns were included in this analysis. Breastfeeding (OR: 1.9; 95% CI: 0.2–15.6) and ankyloglossia (OR: 0.7; 95% CI: 0.3–1.6) were also not associated with LBW (Model 1). Model #2 included all variables with $P < 0.20$ in the bivariate analyzes (Model #1), and the Hosmer and Lemeshow test showed a good adjustment ($P = 0.969$). Thus, Model #2 showed that newborns with mucocele presented a 3.7-fold greater chance (OR: 3.7; 95% CI: 1.1–13.1) of belonging to the LBW group. Likewise, newborns with Epstein pearls presented a 1.8-fold greater chance (OR: 1.8; 95% CI: 1.1–3.2) of belonging to the LBW group, when compared to those newborns without these oral mucosal lesions.

Discussion

This study demonstrated that Epstein pearls and mucocele were more frequent oral mucosal lesions in preterm birth and LBW newborns.

Preterm and LBW have a high collinearity[9] and present similar associated factors. As expected, the main problems arising from high-risk pregnancy are preterm birth and LBW. These factors are unfavorable for postnatal newborn survival.[20] High-risk pregnancy comprises a wide range of clinical and obstetric conditions and may compromise the healthy course of pregnancy.[4,20,21] When there are one or more risk factors

Table 1: Bivariate and multivariate association between gestational age and other variables

Variables	Gestational age		Model 1 No adjusted		Model 2 Adjusted		Model 3 Adjusted	
Full term	Preterm	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	
Newborn sex								
Female	161 (46.7)	31 (42.5)	1	0.513	-	-	-	-
Male	184 (53.3)	42 (57.5)	0.8 (0.5-1.4)		-		-	
High-risk pregnancy								
No	219 (63.7)	31 (42.5)	1	**0.001**	1	**0.020**	1	**0.002**
Yes	124 (36.3)	42 (57.5)	2.3 (1.4-3.9)		2.0 (1.1-3.7)		2.3 (1.3-3.9)	
Type of childbirth								
Vaginal childbirth	219 (85.5)	37 (14.5)	1	**0.040**	1	0.502	-	-
Cesarean birth	125 (77.6)	36 (22.4)	1.7 (1.02-2.8)		1.2 (0.6-2.1)		-	
Breastfeeding								
No	8 (4.2)	3 (4.2)	1	0.383	-	-	-	-
Yes	336 (97.7)	69 (95.8)	0.5 (0.1-2.1)		-		-	
Incubator								
No	299 (86.7)	46 (63.0)	1	**<0.001**	1	**0.002**	1	**<0.001**
Yes	46 (13.3)	27 (37.7)	3.8 (2.1-6.7)		2.7 (1.4-5.1)		3.2 (1.7-5.9)	
NICU								
No	326 (94.5)	59 (80.8)	1	**<0.001**	1	**0.024**	-	-
Yes	19 (5.5)	14 (19.2)	4.7 (1.9-8.5)		2.6 (1.1-6.3)		-	
Infections in newborn								
No	319 (93.0)	70 (95.9)	1	0.369	-	-	-	-
Yes	24 (7.0)	3 (4.1)	0.5 (0.1-1.9)		-		-	
Epstein pearls								
No	214 (62.0)	35 (47.9)	1	**0.027**	1	**0.031**	1	**0.038**
Yes	131 (38.0)	38 (52.1)	1.7 (1.1-2.9)		1.8 (1.1-3.2)		1.7 (1.03-3.0)	
Dental lamina cistys								
No	325 (94.2)	71 (97.3)	1	0.299	-	-	-	-
Yes	20 (5.8)	2 (2.7)	0.4 (0.1-2.0)		-		-	
Bohn's nodules								
No	275 (79.7)	57 (78.1)	1	0.755	-	-	-	-
Yes	70 (20.3)	16 (21.9)	1.1 (0.5-2.0)		-		-	
Mucocele								
No	337 (97.7)	67 (91.8)	1	**0.017**	1	**0.013**	1	**0.017**
Yes	8 (2.3)	6 (8.2)	3.7 (1.2-11.2)		4.9 (1.3-17.8)		4.6 (1.3-16.1)	
Ankyloglossia								
No	294 (85.5)	62 (84.9)	1	0.899	-	-	-	-
Yes	50 (14.5)	11 (15.1)	1.0 (0.5-2.1)		-		-	
Mothers's age (years)								
Up to 19	51 (15.0)	9 (12.3)	1	0.882	-	-	-	-
20-35	241 (70.7)	56 (76.7)	0.9 (0.3-2.5)		-		-	
36 and over	49 (14.4)	8 (11.0)	1.3 (0.6-2.8)		-		-	
Previous health changes								
No	284 (82.3)	54 (74.0)	1	**0.102**	1	0.607	-	-
Yes	61 (17.7)	19 (26.0)	1.6 (0.9-2.9)		1.1 (0.6-2.3)		-	
Sexually transmitted infections								
No	312 (90.4)	64 (87.7)	1	0.477	-	-	-	-
Yes	33 (9.6)	9 (12.3)	1.3 (0.6-2.9)		-		-	
Socioeconomic level								

Contd...

Table 1: Contd...

Variables	Gestational age		Model 1 No adjusted		Model 2 Adjusted		Model 3 Adjusted	
Full term	Preterm	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	
High	89 (25.9)	9 (12.3)	1	**0.016**	1	**0.040**	1	**0.026**
Low	255 (74.1)	64 (87.7)	2.4 (1.1-5.1)		2.2 (1.03-4.9)		2.4 (1.1-5.2)	

Results in bold type are statistical significant at 5% level. Logistic regression model with robust variance for multivariate analyses (Models number 1, 2, and 3). Model 1 Robust model not adjusted; Model 2 All variables with $P<0.20$ in the bivariate analyzes were included in this model. The Hosmer and Lemeshow test was performed ($P=0.467$); Model 3 Type of birth, NICU and previous health change were removed from the analysis for a better adjust of the model. The Hosmer and Lemeshow test was performed ($P=0.708$). NICU: Neonatal intensive care units; OR - Odds ratio; CI - Confidence interval

related to maternal and/or fetal factors, an interaction can be observed between systemic components leading to adverse pregnancy outcomes.[4,20,21] About 15% of pregnant women develop some type of complication during pregnancy. These pregnant women need specific care, as their health status directly influences the fetal health status.[20]

Some studies did not find a significant association between birth weight, gestational age, and oral inclusion cysts.[17,22-24] Another study of 60 preterm and 60 term newborns found that oral inclusion cysts were not associated with prematurity and LBW, but were positively associated with increased gestational age and weight gain.[11] Studies have shown that premature birth can affect craniofacial complex morphology,[6,7] and the shorter the gestational period presented at birth, the greater the risk of congenital changes.[17] Epstein pearls tend to disappear spontaneously soon after birth.[18] A possible hypothesis that justifies the association found in this study is that newborns did not complete adequate gestational weeks for full development and there was not enough time for the remission of these lesions, that is, the more premature the newborn, the greater the chance of Epstein pearls to be present.[9]

Mucocele was associated with prematurity and LBW in the present study. The etiology of mucocele is mainly due to trauma and subsequent obstruction of the salivary glands.[13] Many preterm and LBW infants may be hospitalized in neonatal units and use neonatal intubation. Prolonged or incorrectly placed neonatal intubation can cause palatal groove formation by pressure against the hard palate, infection, laryngeal or tracheal edema, tracheal stenosis, and vocal cord injuries. However, injuries to the oral mucosa are less frequent than injuries to the nasal mucosa.[25] However, our newborns did not undergo neonatal intubation through the oral cavity, but rather through the nose. Other possible causes of mucocele are problems due to breastfeeding,[13] *in utero* thumb sucking, damages in oral mucosa during the passage in the birth canal, and the use of forceps.[26] Moreover, newborns hospitalized at the NICU or at the incubator may be more manipulated than newborns that are discharged from the hospital right after birth. However, one case report showed that mucocele is not frequent in newborns,[27] although the data are not from an epidemiological study. Moreover, the present found a low frequency of mucocele (n = 14 cases, 3.4%).

In fact, preterm and LBW newborns were more hospitalized at the NICU and the incubator. When the health status of the newborn is affected as a result of complications related to maternal and/or fetal health, the newborn may need specific care at the NICU and/or incubator,[18] be it for weight gain, thermal regulation, or cardiorespiratory stability.[28,29]

Ankyloglossia proved not to be associated with prematurity and LBW. In our study, the diagnostic criterion used was that proposed by Martinelli *et al.*[30]

Language development occurs between the 8th and 11th week of gestational period. At this stage, the cells of the frenulum undergo apoptosis and migrate to the median portion of the lingual dorsum. When there is interference in this process, the condition of ankyloglossia is installed.[31] Its relation to breastfeeding is controversial. Some studies relate the occurrence of ankyloglossia to functional problems linked to milk sucking, swallowing, and weight gain.[32,33] Other studies do not support this association between ankyloglossia and breastfeeding.[16,34,35]

The difference in the distribution of preterm newborns and LBW in relation to full-term and NBW newborns can be considered a limiting factor in this study. Future studies should follow-up on newborns to consolidate the results found in this study.

Conclusion

Epstein pearls and mucocele more commonly occurred in preterm and LBW newborns. These lesions can be transient and do not present risks. However, it is necessary to know the clinical characteristics of these lesions so that appropriate management would be performed if clinical interventions are needed. In many cases, the health professional may not identify the

Table 2: Bivariate and multivariate association between birth weight and other variables

Variables	Birth weight		Model 1 No adjusted		Model 2 Adjusted	
	≥2500 g	<2500 g	OR (95% CI)	*P*	OR (95% CI)	*P*
Newborn sex						
Female	166 (84.3)	31 (15.7)	1	0.795	-	-
Male	190 (83.3)	38 (16.7)	0.9 (0.5-1.5)		-	
High-risk pregnancy						
No	223 (87.8)	31 (12.2)	1	**0.009**	1	**0.048**
Yes	133 (78.2)	37 (21.8)	2.0 (1.1-3.3)		1.7 (1.0-3.1)	
Type of childbirth						
Vaginal childbirth	227 (86.6)	35 (13.4)	1	**0.040**	1	0.443
Cesarean birth	128 (79.0)	34 (21.0)	1.7 (1.02-2.8)		1.2 (0.7-2.2)	
Breastfeeding						
No	10 (2.8)	1 (1.4)	1	0.519	-	-
Yes	344 (97.2)	68 (98.6)	1.9 (0.2-15.6)		-	
Incubator						
No	304 (85.9)	50 (72.5)	1	**0.010**	1	0.390
Yes	52 (73.2)	19 (26.8)	2.2 (1.2-4.0)		1.3 (0.6-2.7)	
NICU						
No	339 (86.3)	54 (13.7)	1	**<0.001**	1	**<0.001**
Yes	17 (53.1)	15 (49.9)	5.5 (2.6-11.7)		4.9 (2.1-11.4)	
Infections in newborn						
No	331 (83.8)	64 (16.2)	1	0.819	-	-
Yes	23 (82.1)	5 (17.9)	1.1 (0.4-3.0)		-	
Epstein pearls						
No	222 (86.4)	35 (13.6)	1	**0.072**	1	**0.032**
Yes	134 (79.8)	34 (20.2)	1.6 (0.9-2.7)		1.8 (1.1-3.2)	
Dental lamina cistys						
No	336 (83.6)	66 (95.7)	1	0.670	-	-
Yes	20 (87.0)	3 (13.0)	0.7 (0.2-2.6)		-	
Bohn's nodules						
No	284 (83.5)	56 (16.5)	1	0.793	-	-
Yes	72 (84.7)	13 (15.3)	0.9 (0.4-1.7)		-	
Mucocele						
No	348 (84.7)	63 (15.3)	1	**0.011**	1	**0.040**
Yes	8 (57.1)	6 (42.9)	4.1 (1.3-12.3)		3.7 (1.1-13.1)	
Ankyloglossia						
No	303 (83.2)	61 (16.8)	1	0.476	-	-
Yes	53 (86.9)	8 (13.1)	0.7 (0.3-1.6)		-	
Mothers's age (years)						
Up to 19	55 (87.3)	8 (12.7)	1	0.453	-	-
20-35	244 (81.6)	55 (18.4)	0.6 (0.1-2.0)		-	
36 and over	54 (91.5)	5 (8.5)	1.5 (0.6-3.4)		-	
Previous health changes						
No	287 (84.7)	52 (15.3)	1	0.321	-	-
Yes	69 (80.2)	17 (19.8)	1.3 (0.7-2.4)		-	
Sexually transmitted infections						
No	323 (84.3)	60 (15.7)	1	0.339	-	-
Yes	33 (78.6)	9 (21.4)	1.4 (0.6-3.2)		-	
Socioeconomic level						
High	93 (90.3)	10 (9.7)	1	**0.042**	1	0.070
Low	262 (81.6)	59 (18.4)	2.0 (1.02-4.2)		1.9 (0.9-4.2)	

Results in bold type are statistical significant at 5% level. Logistic regression model with robust variance for multivariate analyses (Models number 1 and 2). Model 1 Robust model not adjusted; Model 2 All variables with $P<0.20$ in the bivariate analyzes were included in this model. The Hosmer and Lemeshow test was performed ($P=0.969$). NICU Neonatal intensive care units; OR - Odds ratio; CI - Confidence interval

presence of oral lesions in newborns or can misdiagnose them with other oral alterations. There may be situations where parents or caregivers may notice the presence of some oral mucosal lesions, resulting in their search for oral health care.[16]

The results found in this study emphasize the relevance of knowing adverse health problems in specific populations. There are situations where oral mucosal lesions can compromise the newborn's performance during breastfeeding. This dysfunction can lead to early weaning.[17] Thus, future studies should investigate oral mucosal lesions as possible risk factors for early weaning.

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Conflicts of interest

There are no conflicts of interest.

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ANEXO F – Registro do protocolo na base de dados PROSPERO

PROSPERO

Systematic Review
1.Review title *
Prevalence of ankyloglossia according to different diagnostic criteria: systematic review of prevalence data
2. Original language title –
3. Anticipated or actual start date *
20/10/2020
4. Anticipated completion date *
31/03/2021
5. Stage of review at time of this submission *

	Started	Completed
Preliminary searches	**Yes**	**Yes**
Piloting of the study selection process	**Yes**	**No**
Formal screening of search results against eligibility criteria	**No**	**No**
Data extraction	**No**	**No**
Risk of bias (quality) assessment	**No**	**No**
Data analysis	**No**	**No**

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12. Funding sources/sponsors *
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13. Conflicts of interest *
None.
14. Collaborators
15. Review Question(s) *
Conduct a systematic review and search for the scientific evidence to indicate whether the prevalence of ankyloglossia varies according to the different diagnostic criteria.

16. Searches *
An electronic and manual search will be performed in the databases: MedLine through ovid, Embase through Elsevier, Scopus, Web of science, Cochrane Systematic reviews, Lilics and BBO through Bireme. Gray literature will be searched through Open gray and Proquest Dissertation & Abstracts.
There will be no language or publication date restriction. The searches will be updated just before the final analyses and further studies retrieved for inclusion.
17. URL to search strategy
18. Condition or domain being studied * - Ankyloglossia
19. Participants/population * - Newborns and infants.
20. Intervention(s), exposure(s) * - Ankyloglossia
21. Comparator(s)/control * - Not apply
22. Types of study to be included initially *
Observational studies (Cross-sectional, cohort, case-control).
The exclusion criteria will be cases / cases series, randomized controlled trials (RCTs), reviews, letters to the editor, narrative reviews and editorials.
23. Context
Studies reporting prevalence data of ankyloglossia will be included.
Individuals taht were submitted to frenectomy or treatment before diagnosis of ankyloglossia will be excluded.
24. Primary outcome(s)*
Diagnosis and prevalence of ankyloglossia
25. Secondary outcomes * - Diagnostic criteria for ankyloglossia
26. Data extraction (selection and coding)
Four independent reviewers will extract data following an abstraction form. Data will be extracted regarding: Country of the authors; year of publication; number of authors; study design; diagnostic criteria for ankyloglossia; country of the patients; age of the children; setting (where are the children from); initial sample size; final sample size; drop-outs; prevalence of ankyloglossia; other systemic conditions (syndromes or any health condition); other oral health problems if reported; frenectomy and/ or frenotomy if reported; problems in breastfeeding if reported; type of funding (industry/ government or university grant/ no); conflict of interest; risk of bias (yes/ no).
27. Risk of bias (quality) assessment *
The quality/risk of bias of the included studies will be evaluated through the Joanna Briggs Institute.
28. Strategy for data synthesis *
29. Analysis of subgroups or subsets *
30. Type of review and method of review *
Type of review
□□Epidemiologic (may include a etiological or observational reviews; and reviews looking at risk or prevalence).
□□Meta-analysis
□□Individual patient data (IPD) meta-analysis
□□Prospective meta-analysis
Health area of review
□□Child health
□□Dental
□□Oral health
□□Public health (including social determinants of health)
31. Language - English
32. Country - Brazil
33. Other registration details
The title of the systematic review will be registered with the Joanna Briggs Institute.
34. Reference and/or URL for published protocol
No I do not make this file publicly available until the review is complete
35. Dissemination plans
Do you intend to publish the review on completion? - Yes
36. Keywords
Ankyloglossia; tongue-tie; prevalence; frenetomy; frenectomy; diagnosis; infant
37. Details of any existing review of the same topic by the same authors
38. Current review status* - Review Ongoing
39. Additional information
40. Details of final report/publication(s)