UNIVERSIDADE FEDERAL DE PELOTAS
Faculdade de Odontologia
Programa de Pós-Graduação em Odontologia

Tese

Lesões de mucosa bucal em estudos de base populacional: revisão sistemática e estudo transversal em gestantes.

Karine Duarte da Silva

Pelotas, 2018

Karine Duarte da Silva

Lesões de mucosa bucal em estudos de base populacional: revisão sistemática e estudo transversal em gestantes

Tese apresentada ao Programa de Pós-Graduação em Odontologia da Faculdade de Odontologia da Universidade Federal de Pelotas, como requisito parcial à obtenção do título de Doutor em Odontologia, área de concentração Clínica Odontológica, ênfase em Diagnóstico Bucal.

Coorientadora: Profa. Dra. Sandra Beatriz Chaves Tarquinio

Coorientadores: Prof. Dr. Marcos Britto Correa

Prof. Dr. Flávio Fernando Demarco

Pelotas, 2018

Universidade Federal de Pelotas / Sistema de Bibliotecas
Catalogação na Publicação

S586l Silva, Karine Duarte da

Lesões de mucosa bucal em estudos de base populacional : revisão sistemática e estudo transversal em gestantes. / Karine Duarte da Silva ; Sandra Beatriz Chaves Tarquinio, orientadora ; Marcos Britto Correa, Flávio Fernando Demarco, coorientadores. — Pelotas, 2018.

78 f. : il.

Tese (Doutorado) — Programa de Pós-Graduação em Diagnóstico Bucal, Faculdade de Odontologia, Universidade Federal de Pelotas, 2018.

1. Prevalência. 2. Doenças da boca. 3. Gestantes. 4. Métodos. 5. População. I. Tarquinio, Sandra Beatriz Chaves, orient. II. Correa, Marcos Britto, coorient. III. Demarco, Flávio Fernando, coorient. IV. Título.

Black : D6

Elaborada por Fabiano Domingues Malheiro CRB: 10/1955

Karine Duarte da Silva

Lesões de mucosa bucal em estudos de base populacional: revisão sistemática e estudo transversal em gestantes

Tese apresentada, como requisito parcial, para obtenção do grau de Doutor em Odontologia, Programa de Pós-Graduação em Odontologia, Faculdade de Odontologia de Pelotas, Universidade Federal de Pelotas.

Data de Defesa: 09/07/2018

Banca examinadora:

Profa. Dra. Sandra Beatriz Chaves Tarquinio (presidente)

Doutora em Patologia Bucal pela Universidade de São Paulo – São Paulo

Profa. Dra. Ana Carolina Uchoa Vasconcelos

Doutora em Estomatologia pela Pontifícia Universidade Católica do Rio Grande do Sul

Profa. Dra. Ana Paula Neutzling Gomes

Doutora em Patologia Bucal pela Universidade de São Paulo – São Paulo

Profa. Dra. Andréa Homsi Dâmaso

Doutora em Ciências pela Universidade Federal de Pelotas

Profa. Dra. Adriana Etges (suplente)

Doutora em Patologia Bucal pela Universidade de São Paulo – São Paulo

Profa. Dra. Fernanda Nedel (suplente)

Doutora em Biotecnologia pela Universidade Federal de Pelotas

Dedico este trabalho ao meu grande amigo
Wellington Luiz da Rosa

Agradecimentos

Agradeço primeiramente à **Universidade Federal de Pelotas (UFPel),** em nome de seu Magnífico Reitor Pedro Hallal**,** e à **Faculdade de Odontologia** da UFPel, em nome de sua Ilma. Sra. Diretora Adriana Etges, pelo ensino de excelência concedido. Ao **Programa de Pós-Graduação em Odontologia** da UFPel, em nome de sua coordenadora Profa. Dra. Tatiana Pereira Cenci, por proporcionar aos seus alunos diversas oportunidades acadêmicas ao longo do mestrado e do doutorado.

À minha orientadora **Profa. Dra. Sandra Beatriz Chaves Tarquinio**, por ter compartilhado comigo seus conhecimentos, pelas oportunidades acadêmicas concedidas, pelo apoio sempre presente nas minhas decisões, e pelo vínculo de amizade que se fortaleceu nos últimos anos.

Aos meus coorientadores **Prof. Dr. Marcos Britto Correa**, por ter me acolhido e orientado com tanta disponibilidade, e ao **Prof. Dr. Flávio Fernando Demarco**, em especial pela oportunidade de participação nos estudos de coorte de Pelotas.

À banca examinadora pelo aceite do convite de contribuírem com esse trabalho.

Às professoras **Adriana Etges**, **Ana Carolina Uchoa Vasconcelos** e **Ana Paula Neutzling Gomes** por terem contribuído muito na minha formação por meio de seus ensinamentos e exemplos. Foi muito bom ter convivido e crescido com vocês ao longo desses 8 anos.

Ao **Centro de Diagnóstico das Doenças da Boca da FOUFPel**, minha segunda casa por longos anos, local onde fiz amigos e que me possibilitou executar diversas atividades científicas.

Ao **Centro de Pesquisa em Saúde Dr. Amilcar Gigante** da UFPel, pela oportunidade de participar dos estudos de coorte e pela disponibilidade de acolher alunos de diversas aulas para as disciplinas modulares que oferece.

À **Faculdade de Odontologia da Universidade Federal de Minas Gerais**, em especial à Profa. Dra. Maria Cássia Ferreira de Aguiar, Profa. Dra. Patrícia Carlos Caldeira e Prof. Dr. Ricardo Alves de Mesquita pela acolhida, pela partilha de conhecimentos e pelos exemplos profissionais que são para mim.

À **CAPES**, **CNPq** e **FAPERGS** pelas bolsas de estudo e auxílios à pesquisa concedidos desde o período da iniciação científica até o doutorado.

Aos **alunos** que coorientei durante a pós-graduação, em especial Lauren Schuch, hoje pós-graduanda, e Êmile de Morais. Vocês foram e ainda são essenciais na minha formação como docente e pesquisadora, fazem-me refletir sobre esse processo, e estão sempre prontas para ajudar nessa caminhada que felizmente não trilhamos sozinhos.

Aos meus queridos **amigos** pelotenses, em especial Wellington Luiz, Roberta Escher, Lucas Brondani, Juan Pablo Aitken, Cácia Signori, Alexandra Cocco, Verônica Lima, Giordana Boteselle e Karen Flores. Juan, pelos momentos partilhados como colega de doutorado e amizade sincera. Wellington, a dedicatória deste trabalho fala por si só, obrigada por existir e fazer da minha existência mais completa, você é muito especial!

Não menos importante, aos **amigos** que fiz durante minha estada em Belo Horizonte, em especial Mariana Israel, Natália Cardoso, Patrícia Junqueira, Andreza Cardoso e Júlia Catarina, pela acolhida, pelo carinho e pelos momentos de alegria compartilhados. Mariana, por ter fortalecido minha Fé.

À minha **família**, que sempre me apoiou, orientou e deu o suporte necessário para a realização dos meus sonhos. Mãe e pai, a vocês o amor em dobro do que recebo e a gratidão por serem meu porto seguro, amo vocês!

Assim, termino meus agradecimentos com a seguinte frase:

“A gratidão é o sentimento que mais aproxima o homem de Deus” (Miguel de Cervantes).

Notas Preliminares

A presente tese foi redigida segundo o Manual de Normas para Dissertações, Teses e Trabalhos Científicos da Universidade Federal de Pelotas de 2013, adotando o Nível de Descrição em Capítulos não convencionais descrita no Apêndice D do referido manual. <http://sisbi.ufpel.edu.br/?p=documentos&i=7> Acesso em: 7 mai. 2018.

Resumo

SILVA, Karine Duarte da. **Lesões de mucosa bucal em estudos de base populacional: revisão sistemática e estudo transversal em gestantes.** 2018. 79f. Tese de Doutorado em Odontologia - Programa de Pós-Graduação em Odontologia. Universidade Federal de Pelotas, Pelotas, 2018.

Estudos de base populacional que avaliem a prevalência de lesões de mucosa bucal (LMBs) são infrequentes na literatura. Normalmente são realizadas análises transversais conduzidas em serviços especializados, fato que, associado à diversidade de metodologias empregadas, dificulta as comparações entre os estudos. O objetivo desse trabalho foi realizar uma revisão sistemática para avaliar aspectos metodológicos de estudos de base populacional sobre prevalência de LMBs, além de investigar a prevalência dessas lesões em um estudo com gestantes. Na revisão, as bases de dados Pubmed, Web of Science e Scopus foram pesquisadas. Dados referentes à tamanho da amostra, sexo e idade dos sujeitos, critérios diagnósticos utilizados, características das lesões, e medidas de concordância entre os examinadores foram extraídos dos estudos e analisados descritivamente. No estudo transversal de base populacional, as gestantes responderam a um questionário e receberam exame clínico bucal. Diagnósticos clínicos e características das LMBs foram coletados, além de histórico odontológico. Os dados foram analisados descritivamente no programa STATA versão 12.0. Foram incluídos 29 estudos na revisão sistemática, sendo observada falta de padronização das metodologias, principalmente em relação a critérios diagnósticos, treinamento e calibração dos examinadores, adequada taxa de resposta e apropriada apresentação dos resultados. Das 2481 gestantes incluídas no estudo transversal, 409 (16.49%) apresentavam LMBs, Os diagnósticos clínicos mais frequentes foram exostose (79-16.39%), língua saburrosa (70-14.52%), e pigmentação acastanhada oral benigna (65-13.49%). Quando agrupados, alterações de desenvolvimento, pigmentações acastanhadas orais de caráter benigno e doenças infecciosas, representadas principalmente por parúlides, foram os grupos mais prevalentes, em ordem decrescente. Quase 50% das mulheres nunca realizou autoexame oral e mais de 86% afirmaram não ter recebido orientação sobre higiene bucal durante a gestação. Concluiu-se que os pouco estudos de base populacional sobre prevalência de LMBs apresentam deficiências em suas metodologias. O estudo realizado com as gestantes, apesar de revelar uma prevalência relativamente baixa de LMBs, utilizou metodologia padronizada e foi o primeiro estudo a fornecer dados sobre a ocorrência desse desfecho em mulheres grávidas.

Palavras-chave: prevalência; doenças da boca; gestantes; métodos; população

Abstract

SILVA, Karine Duarte da. **Oral mucosal lesions in population-based studies: systematic review and cross-sectional study in pregnant women.** 2018. 79f. PhD in Dentistry. Graduate Program in Dentistry. Federal University of Pelotas, 2018.

Population-based studies evaluating the prevalence of oral mucosal lesions (OMLs) are uncommon in the literature. Cross-sectional analyzes conducted in specialized services are usually carried out, which, in combination with the diversity of methodologies used, makes difficult the comparisons between studies. The objective of this study was to perform a systematic review to evaluate methodological aspects of population-based studies on the prevalence of OMLs, in addition to investigating the prevalence of these lesions in a study with a cohort of pregnant women. In the review, Pubmed, Web of Science and Scopus databases were searched. Data regarding sample size, sex and age of the subjects, diagnostic criteria used, lesion characteristics, and measures of agreement among the examiners were extracted from the studies and analyzed descriptively. In the cross-sectional population-based study, the pregnant women answered a questionnaire and received oral clinical examination. Clinical diagnoses and characteristics of OMLs were collected, as well as dental history. The data were analyzed descriptively in the STATA program version 12.0. Twenty-nine studies were included in the systematic review, being observed a lack of standardization of methodologies, especially regarding diagnostic criteria, training and calibration of the examiners, adequate response rate and appropriate presentation of the results. Of the 2481 pregnant women included in the cross-sectional study, 409 (16.49%) had OMLs. The most frequent clinical diagnoses were exostoses (79-16.39%), coated tongue (70-14.52%), and benign oral brownish pigmentation (65-13.49%). When grouped, developmental alterations, benign oral brownish pigmentations and infectious diseases, represented mainly by parulides, were the most prevalent groups, in descending order. Almost 50% of women never performed oral self-examination and more than 86% reported no oral hygiene orientation during gestation. It was concluded that the few population-based studies on the prevalence of OMLs present deficiencies in their methodologies. The study performed with pregnant women, despite of revealing a relatively low prevalence of OMLs, used standardized methodology and was the first study to provide data on the occurrence of this outcome in pregnant women.

Key-words: prevalence; mouth diseases; pregnant women; methods, population

Sumário

1 Introdução

A saúde bucal é parte integrante e essencial da saúde geral das pessoas. Disfunções na fonação, mastigação e deglutição podem estar associadas à presença de alterações bucais, que podem causar desconforto, dor, xerostomia e alterações no paladar, prejudicando as funções normais do indivíduo e afetando sua qualidade de vida (OLIVEIRA et al., 2015; SULIMAN et al, 2012; VILLANUEVA-VILCHIS et al., 2016).

Dentre as desordens que acometem a cavidade bucal encontram-se as lesões de tecidos moles ou de lesões de mucosa bucal (LMBs). Em sua maioria, as LMBs são representadas por condições indolentes como língua fissurada, ulceração aftosa recorrente, úlcera traumática e queilite angular, entretanto lesões potencialmente malignas e malignas de boca também podem ser encontradas, especialmente em países como a Índia em que o consumo de tabaco é alto, associado ao de álcool (BYAKODI et al., 2011; FENG et al., 2015; REDDY et al., 2015).

A prevalência de LMBs é difícil de ser estabelecida apropriadamente, pois existem poucos estudos de base populacional que fazem essa avaliação (DOST, DO, FARAH, 2016; FENG et al., 2015; HAAS et al., 2015; HOLDE et al., 2016; REDDY et al., 2015). Os estudos epidemiológicos sobre o tema são majoritariamente de base de serviço, ou seja, utilizam amostras de conveniência de serviços especializados (ALI et al., 2012; PESSOA et al., 2015). Apesar da sua relevância em termos de validade interna, não representam a distribuição desse grupo de patologias na população em geral, uma vez que são selecionados apenas os pacientes que procuraram os serviços médico-odontológicos (KOAY et al., 2010; PESSOA et al., 2015) ou aqueles que sofreram procedimento cirúrgico oral e tiveram material de biópsia enviado para análise histopatológica (LIMA et al., 2008; ALI et al., 2012).

Nota-se que a prevalência de LMBs ao redor do mundo é extremamente heterogênea, devido às diferenças observadas entre as distintas faixas etárias e

ao predomínio de algumas enfermidades sobre outras em diferentes regiões do globo (AL-MAWERI et al., 2015; BYAKODI et al., 2011). Um estudo de base populacional realizado com 901 adultos indianos revelou que 44,1% apresentava LMBs, das quais 22,8% eram fibrose submucosa oral, 8% leucoplasia e 2,7% câncer oral, lesões intimamente relacionadas ao hábito de mascar tabaco nessa população (REDDY et al., 2015). Devido à presença deste hábito, também do consumo de álcool, lesões pré-malignas e malignas bucais são frequentemente relatadas na Índia (BYAKODI et al., 2011; REDDY et al., 2015).

Tarquinio e cols (2013), em análise conduzida com 720 indivíduos pertencentes a uma coorte de nascimentos de base populacional em Pelotas, Brasil, encontraram uma prevalência de 23,3% lesões bucais em indivíduos com 24 anos de idade, sendo que 19,4% deles apresentavam mais de uma lesão. A ocorrência dessas condições mostrou-se associada a baixo nível socioeconômico ao nascimento, falta de instrução de higiene oral por um dentista até os 15 anos e hábito de fumar aos 22 anos.

Alterações relacionadas a fatores como trauma, irritação local ou deficiência do sistema imunológico são frequentes em populações mais jovens e crianças (CHEN et al., 2010; OLIVEIRA et al., 2015). Porém, lesões pré-malignas e malignas, como queilites actínicas, leucoplasias, eritroplasias e carcinoma espinocelular são raras nestes grupos, uma vez que possuem caráter crônico a partir da exposição prolongada a fatores de risco como tabaco, álcool e radiação solar (BYAKODI et al., 2011; LUCENA et al., 2012). Além disso, lesões como o granuloma piogênico, por exemplo, segundo a literatura podem ocorrer com maior frequência em mulheres grávidas (RAMOS E SILVA et al., 2016; CARDOSO et al., 2013), entretanto investigações sobre a ocorrência de LMBs nesse grupo são escassas (CARDOSO et al., 2013; KRISHNAPILLAI et al., 2012), senão ausentes, quando se trata de estudo de base populacional.

Outro aspecto que dificulta a comparação entre os estudos, são as diferenças nas metodologias empregadas para a determinação da prevalência de LMBs. Distintos critérios diagnósticos tem sido utilizados na condução do exame clínico bucal dos indivíduos em estudos epidemiológicos sobre LMBs, sendo que a maioria das investigações empregam os critérios da Organização Mundial da Saúde (OMS) (KRAMER et al., 1980), que se baseiam em

diagnósticos clínicos específicos (BYAKODI et al., 2011; GHENO et al., 2015). Alguns estudos complementam os critérios da OMS com os critérios descritos por Axéll et al. (1996) para lesões brancas de tecidos moles (AL-MAWERI et al., 2015 ; BHATNAGAR et al., 2013). Existem ainda estudos que classificam as LMBs de acordo com a lesão fundamental: úlcera, mancha vermelha, mancha acastanhada/enegrecida, placa branca, erosão, pápula/nódulo, vesícula/bolha (SULIMAN et al., 2012; TARQUINIO et al., 2013). Nota-se, dessa forma, a falta de padronização dos critérios diagnósticos para determinação da prevalência de LMBs. Ressalta-se também a ausência de treinamento e calibração dos entrevistadores e examinadores em alguns estudos (FENG et al., 2015; JAHANBANI et al., 2012) e sua presença em outros, com valor satisfatório de reprodutibilidade entre eles (DO et al., 2014; TARQUINIO et al., 2013).

Além disso, determinadas patologias podem ter ocorrência subestimada ou superestimada. Alterações de desenvolvimento como língua geográfica, língua fissurada, exostoses e grânulos de Fordyce são coletadas em alguns estudos (FENG et al., 2015; JAHANBANI et al., 2012) e em outros não (TARQUINIO et al., 2013; OLIVEIRA et al., 2015), relatando-se que não se tratam de verdadeiras patologias e que, em sua maioria, não apresentam significado clínico relevante (TARQUINIO et al., 2013). Outro aspecto interessante refere-se à resolução rápida observada em determinados processos patológicos, como úlcera traumática, ulceração aftosa recorrente e infecção herpética secundária, fazendo com que a prevalência maior ou menor dessas patologias bucais nas populações dependa da sua presença no momento do exame clínico (FENG et al., 2015; JAHANBANI et al., 2012).

Não obstante as dificuldades relatadas, estudos acerca da prevalência de LMBs em diferentes populações são de extrema importância, visto que fornecem dados sobre as lesões mais frequentes, favorecendo a tomada de medidas preventivas e o esclarecimento dos fatores de risco envolvidos com tais condições. Nesse contexto, estudos de base populacional são de grande utilidade, especialmente os longitudinais, que possibilitam a investigação de relações causais e a observação de condições patológicas de desenvolvimento crônico (PERES et al., 2008).

Considerando estes aspectos, ganham relevância os estudos de

acompanhamento realizados na cidade de Pelotas, Rio Grande do Sul, Brasil, em coortes de nascidos vivos (BARROS et al., 2008; HALLAL et al., 2017). As LMBs foram incluídas como um dos desfechos investigados nos estudos de coorte de Pelotas, avaliando indivíduos com 24 anos de idade pertencentes à coorte de 1982, e com 5 anos de idade, da coorte de 2004 (OLIVEIRA et al., 2015; TARQUINIO et al., 2013). Mais recentemente, as gestantes mães dos indivíduos pertencentes à coorte de nascimentos de 2015 (HALLAL et al., 2017) foram avaliadas no pré-natal, obtendo-se dados de saúde geral e bucal, entre eles sobre a prevalência de LMBs.

Mulheres gestantes representam um grupo específico não só em relação à condição gestacional, destacando-se mudanças biológicas importantes, como também relacionado a comportamentos, hábitos, desordens psicológicas e, não raro, aspectos ligados à saúde bucal (CARDOSO et al., 2013; FIGUERO et al., 2013; RAMOS E SILVA et al., 2016; SMEDBERG et al., 2015). Cárie e doença periodontal podem ser favorecidas nesse período quando se tem uma combinação de fatores locais e alterações hormonais associadas ao aumento dos níveis inflamatórios, entre eles da inflamação gengival, e diminuição da resposta ao biofilme bacteriano (CARDOSO et al., 2013; FIGUERO et al., 2013). Similarmente, essas mesmas alterações sistêmicas e locais podem predispor ao desenvolvimento de LMBs nesse grupo de indivíduos. O granuloma piogênico, por exemplo, também conhecido como granuloma gravídico, é uma lesão benigna com diversos relatos de ocorrência em grávidas, e representa uma resposta inflamatória exacerbada a irritantes locais como trauma e biofilme bacteriano, sendo postulado que em mulheres no período gestacional possa ocorrer até mesmo sem presença considerável de placa dentária (CARDOSO et al., 2013; FIGUERO et al., 2013; RAMOS E SILVA et al., 2016).

Até o momento, são ausentes na literatura estudos de base populacional sobre a prevalência de LMBs em gestantes, por isso a relevância do estudo conduzido em Pelotas com essas mulheres. Além disso, tendo em vista o número limitado de estudos epidemiológicos de base populacional que avaliam LMBs e as diferenças encontradas nas metodologias empregadas, seria interessante sistematizar dados referentes ao delineamento e condução dos mesmos, buscando-se observar aspectos importantes de serem incluídos em

estudos sobre prevalência de LMBs, e visando auxiliar os pesquisadores no desenho metodológico de estudos com maior padronização e possibilidade de comparação com outros trabalhos semelhantes na literatura.

Dessa forma, o objetivo do presente trabalho é fazer uma revisão sistemática da literatura sobre estudos de base populacional acerca da prevalência de LMBs, visando observar aspectos metodológicos dos mesmos; além de investigar a prevalência de LMBs em um grupo populacional de gestantes.

2 Capítulo 1

METHODOLOGICAL ASPECTS OF POPULATION-BASED STUDIES ON PREVALENCE OF ORAL MUCOSAL LESIONS: A SYSTEMATIC REVIEW

Karine Duarte da Silva[1*], Wellington Luiz de Oliveira da Rosa[1], Juan Pablo Aitken Saavedra[1], Rafael Sarkis-Onofre[2], Flávio Fernando Demarco[1], Marcos Britto Correa[1], Sandra Beatriz Chaves Tarquinio[1]

[1]Graduate Program in Dentistry – Federal University of Pelotas – Pelotas, Brazil
[2]Graduate Program in Dentistry – Meridional Faculty/IMED – Passo Fundo, Brazil

*Corresponding author:

Karine Duarte da Silva

ORCID: 0000-0002-1451-7727

Address: Gonçalves Chaves Street, 457 (room 607), Pelotas, RS, Brazil, 96015560

Phone number: +55 53 32602801

Email address: karineduartedasilva1@gmail.com

O artigo será submetido à revista *Community Dentistry and Oral Epidemiology* (Qualis A1; Fator de Impacto: 1.992) e está formatado segundo as normas do periódico.

ABSTRACT

Objective: The aim of this study was to conduct a systematic review of the literature to evaluate methodological aspects of population-based studies about oral mucosal lesions prevalence.

Methods: Two reviewers independently conducted the literature search in three databases (Pubmed/MEDLINE, Web of Science and Scopus) and extracted data using a standardized form. The following characteristics of the studies included were collected: sample size and subjects, diagnostic criteria, type, grouping and characteristics of the lesions, lesions excluded, and measures of agreement between examiners. Data were analyzed descriptively, being performed a data synthesis of each included study. Quality analysis of the studies was done and the risk of bias was evaluated.

Results: A total of 29 studies were included in the qualitative analysis. The diagnostic criteria are in accordance with World Health Organization guides in most of them, but a number of other references were used, impairing the standardization and reproducibility of the studies. Just over half analyzed the concordance between examiners, and most of them did not show adequate response rate and presentation of results with appropriated confidence intervals.

Conclusions: There is a lack of standardization between studies about OMLs prevalence. There are important points that should be improved mainly regarding diagnostic criteria, training of examiners, adequate response rate and presentation of the results, aiming to augment the quality, realibility, reproducibility and comparision between studies in this field.

Keywords: mouth diseases, mouth mucosa, epidemiology, prevalence, methods, population

INTRODUCTION

The term oral mucosal lesions (OMLs) refers to any abnormal change in the oral mucosa related to color, surface aspect, swelling or loss of its integrity[1]. They can comprise pathologies and developmental defects, some of them quite common in the oral cavity, such as fibromas, mucoceles, candidiasis, leukoplakias, geographic and/or fissured tongue, Fordyce granules, and not so rarely oral cancer[2-4]. It is important to emphasize that this large group of alterations may include entities with relevant clinical implications, such as pain, difficulties in eating, speeching and also aesthetic problems, which may reflect on individuals oral health-related quality of life[5,6]. The prevalence of OMLs in general population globally varies significantly across different regions and countries, ranging from 4.9% to 64.7%[1].

Epidemiologic studies on OMLs are not so frequent in comparison with similar studies on caries and periodontitis[1,7]. The literature is rich in case reports, case series and cross-sectional studies on OMLs conducted in specific settings[8-10]. Most of the latter uses convenience samples collected from specialized services in dentistry and medicine[8,11], and still those from oral pathology reference centers[10,12]. These types of studies are important to understand the service profiles in relation to the frequency and characteristics of OMLs, however it is not possible extrapolate their results for the whole population. Painful lesions, for example, can be overestimated in these studies, since the individuals search the services more frequently[4,13]. Similarly, some lesions need histopathological analysis to confirm the diagnosis, so, when only the cases from biopsies are evaluated, some entities are not found, since their diagnosis and treatment are based on clinical approach[8,12.]

On the other hand, observational studies conducted in a random sample or whole population allow to know more reliably the prevalence and characteristics of the lesions under investigation[2,4,14]. Biases usually found in studies using convenience samples can be reduced in population-based studies. For this reason, the latter are usually more consistent and brings more specific results to the reality of the population as a whole[15,16].

Considering the methodology applied to conduct the observational studies, some important aspects have to be pointed, such as the use of well-known tools and well-established criteria, such as those for diagnosis, inclusion and exclusion of lesions, how to group them, and also how to analyze the concordance between examiners[2,5,17]. The standardization of these aspects favors the understanding of the study and application of

its results as well as their reproduction[16]. In this way, it is not recommended to evaluate service-based and population-based observational studies on the prevalence of OMLs jointly, as well as making comparisons between them. Differences in methodologies between these types of studies, such as sample selection, diagnostic criteria, the included lesions, and other aspects end up hindering the systematic analysis of the studies[1,2,7]. Therefore, this systematic review aims to analyze population-based studies on OMLs prevalence in relation to its methodological aspects, seeking for observing how they are being performed and also aiming to produce evidence that may contribute to more consistent and standardized studies.

METHODS

This review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA Statement)[18]. The research question was: "How are population-based studies of oral mucosal lesions (OMLs) being conducted regarding methodological aspects?"

Eligibility criteria

We included population-based epidemiological studies on prevalence of OMLs which mentioning in the methodology the tools and criteria used to conduct the study. We excluded review articles, case reports, case series and pilot studies. Also, studies evaluating only intraosseous and/or dental and periodontal oral lesions (gingivitis and periodontitis), studies about OMLs in specific sites, such as gum and tongue, studies with already ill individuals (systemic disease) and/or suffering radiotherapy treatment, service-based studies and articles in a language other than English were excluded.

Electronic searches

Searches were performed in three databases (PubMed/MEDLINE), Web of Science and Scopus without period restriction. Initially, the search strategy was developed for PubMed (MEDLINE) and adapted for other databases (Appendix A). References cited in the included articles were also reviewed to identify any further relevant articles. Literature searches were carried out by two independent reviewers until 12th January 2018.

Study selection

The results of literature searches were imported into Endnote X1 software (Thompson Reuters, Philadelphia, PA, USA) to remove duplicates. Two authors independently assessed the titles and abstracts of all of the documents. Initially, full copies of all of the potentially relevant studies were identified. Those appearing to meet the inclusion criteria or those which show insufficient data in the title and abstract to make a clear decision were selected for full analysis. Full-text papers were assessed independently and in duplicate by reviewers. Any disagreement was resolved through discussion and consensus or by a third reviewer. Only studies that fulfilled all of the eligibility criteria were included.

Data extraction and syntesis

The data of each included study were extracted in duplicate by two reviewers using a standardized form. The reviewers previously discussed the whole aspects of the review that would be collected from the studies, and any disagreement was resolved through discussion and consensus or by a third reviewer.

The data were analyzed descriptively, and the following data of the included studies were extracted in order to perform a data synthesis of each study:

- Author, year of publication, country, sample size and study design including age and sex of participants.
- Methodological aspects: diagnostic criteria, type, grouping and characteristics of the lesions, lesions excluded, and measures of agreement between examiners.
- Important data collected related to the patients such as ethnicity, occupation, income, smoking and drinking habits, medication use, among others were also tabulated.

Quality of included studies

The full text of all studies was assessed for methodological quality according to a score system devised by Loney *et al.*[19] and indicated for population-based studies[20]. One reviewer independently assessed the studies based on eight items of this scoring[19], as follows: 1) random sample or whole population; 2) unbiased sampling frame; 3) adequate

sample size; 4) measures were the standard; 5) outcomes measures by unbiased assessor; 6) adequate response rate; 7) confidence intervals (CIs), subgroup analysis; 8) study subjects described. Each item may receive a score 0 (not score) or 1, therefore the total score for each study can reach a minimum value of 0 and a maximum of 8.

RESULTS

Search strategy

A total of 5090 potentially relevant records were identified from all of the databases. Seven additional studies were identified as relevant from a reference list survey. Of the 4107 articles remaining after duplicates removed, 4060 were excluded in a title and abstract examination, because they did not meet the eligibility criteria. Of the 47 studies retained for detailed review, 18 were not included because 14 were not population-based studies, 2 studies in which OMLs prevalence was not the objective, 1 study using the same sample of another main study already included and 1 study that was available only as a thesis. The list of these excluded articles is available as Appendix B. A total of 29 studies fulfilled the selection criteria and were included in the qualitative analysis. Fig. 1 is a flowchart that summarizes the article selection process according to the PRISMA Statement[18].

Descriptive analysis

Table 1 shows the characteristics of included studies. The first included study has been published in 1963[22] and the last two in 2015[1,5]. Eighteen (62.1%) studies were published in the 21st century[1,2,4,5,12,14,15, 17,22-31]. Countries from Asia accounting for 8 studies[1,17,25-28,33,34], Europe[22,28,29,30,34-36] and South America[4,5,17,21,23,31,37] for 7 each, and North America for 5[13,14,38-40]. Australia[2] in Oceania and Nigeria[41] in African continent are responsible for 1 study each.

The sample size ranged between 118[22] individuals and 39,206[38]. Four studies are part of larger investigations related to general and oral health: Australian National Survey of Adult Oral Health[2], Third German Oral Health Study[29] and Third National Health and Nutrition Examination Survey[12,14]. Similarly, three studies are cross-sectional analysis nested in cohorts conducted in Brazil[4,5] and Sweden[35].

Only one study did not include both sexes, being conducted only with men[22]. In

relation to the age group of the participants, studies with children and adolescents (until 24 years)[44] corresponding to 9 (31.0%)[5,14,25,28,31,37,38,40,41] and adults to 12 (37.9%)[4,12,22-24,26,29,32,33,35,39]. Eight studies (17.2%) were conducted with both children or adolescents and adults[2,15,17,30,37], and four (13.8%)[1,21,27,34] without determination of age.

The majority of the included studies investigated all types of OMLs, however two (6.9%) evaluated only precancerous oral lesions[15,34] and they were included because the importance of this group of lesions in the context of OMLs. Four studies (13.8%)[21,37,40,41] analyzed only oral or orodental anomalies such as commissural lip pits, Fordyce granules, fissured and geographic tongue, among others. The lesions analyzed in the studies were grouped in 14 (48.3%)[1,2,4,5,12,14,17,24,26,27,30,34-36] of them.

In terms of examiners' training and data collection, most of the studies (23 – 79.3%) used World Health Organization guidelines, or researches published by the renowned Tony Axéll and colleagues toward the years, or both. Moreover, six studies (20.7%)[29,30,34,35,36,38] used Roed-Petersen & Renstrup[43] for the classification of lesions in intraoral sites.

Importantly, only three studies (10.3%) recorded data on size[4,5,14], surface morphology[14], color[14], consistency[14], associated symptoms[4,14], and duration[4,14] of the lesions. Three studies (10.3%)[2,4,5] did not use clinical diagnoses to classify the lesions and considered the fundamental type of them such as plaque, papule/nodule, vesicle/blister, erosion and ulcer.

Most of studies did not mention excluded lesions, but three (10.3%) of them[4,5,23] related that developmental defects and/or some lesions such as petechiaes[4,5] were not included. Two studies (6.9%)[25,28] reported that recurrent herpetic lesions and aphthous stomatitis were recorded only if observed at the time of examination. Moreover, one study (3.4%)[28] excluded periodontal and gingival diseases.

Relating to interobserver and/or intraobserver reliability of clinical assessments in the calibration phase, 15 studies (51.7%)[2-4,5,17,21,23,24,26,28,29,31-33,38] have performed this evaluation, but five of them did not mention the kappa value found[2,3,21,28,38]. For the others, the figures ≥0.6 indicated that interobserver and/or intraobserver agreement was substantial or good.

Finally, other data collected and related to schooling, occupation, daily habits, oral self-examination, medication use, systemic diseases, among many other individual features, can be seen in Table 1.

Quality of Reviewed Studies

Relating to the assessment of methodological quality, included studies presented a high risk of bias in items "Is the response rate adequate? Are the refusers described?" and "Are the estimates of prevalence or incidence given with confidence intervals and in detail by subgroups, if appropriate?" (Fig. 2).

DISCUSSION

This systematic review highlight the major weaknesses of population-based studies on OMLs prevalence. The point of interest was the methodologies of these studies, being observed that the deficiencies are mainly related to the sample selection, use of well-established diagnostic criteria, training and blindness of the evaluators, and presentation of the results. Overall, can be stated that there is a lack of standardization of studies in this field, which makes difficult to compare them and affects their reliability.

The literature pointed conditions that give a study of OMLs prevalence greater quality, internal and external validity, such as larger probability sample, standard definitions of lesions of interest, calibrated and blinded interviewers and examiners, presentation of standard errors or 95% CI of the results and low number of missing data[4,14,16]. In this sense, the marked variation in the prevalence of OMLs between studies may be due to differences in methodologies and clinical diagnostic criteria applied, as well as geographic settings and socio-demographic characteristics[16,28].

In a comparative analysis of OMLs prevalence studies, the main difficulty is to evaluate population-based and service-based studies together. For this reason, the focus of this review is only the population-based studies. These last ones may show greater reliability and the possibility of the extrapolation of their results into the general population[4,16]. Overall, the literature is devoid of credible population-based data on OMLs[1], although World Health Organization encourages this type of publication for these oral conditions[43].

The difficulty of conducting population-based studies is known, in terms of both logistics and costing[14,43]. In this sense, it was observed that OMLs studies with larger samples had government funding and were part of major investigations conducted not only on oral health, but also on systemic health. For example, the National National Survey of Adult Oral Health[2], Third German Oral Health Study[29], Third National Health and Nutrition Examination Survey[14], and the renowned cohort studies conducted in Pelotas (Brazil)[44]. It is interesting to observe that, in spite of the small number, Asian countries published eight population-based studies on the prevalence of OMLs, including oral cancer. In some of them, as in India, the population chews tobacco in addition to smoking tobacco, habits related to the development of oral cancer[15]. Just below in the ranking with 7 published studies is Europe and South America, followed by North America with 5. Considering the countries that published the most in the Americas, Brazil published 4 articles on the theme and United States of America 3. These differences between continents may reflect the importance that they give to the topic and the economic and logistic conditions to carry out the population-based studies.

When analyzed only population-based studies about OMLs prevalence, it can be observed that some of them have restricted the investigation to specific groups of individuals or diseases[15,22,34]. Campisi et al.[22] stated that the decision to select only men was based on the fact that they represented in Italy a group at higher risk for the development of oral cancer than women. However, the inclusion of both men and women in the study could show more comprehensively the prevalence of OMLs in the whole population. Similarly, some studies have chosen to investigate only lesions with malignant transformation potential, such as leukoplakia and lichen planus[15,34]. In fact, these conditions have a relevant clinical interest whereas they may be associated with the development of oral cancer and, in terms of public health, the importance of oral cancer prevention and detection is widely recognized[4,15].

Regarding the divisions observed in studies between children and adults, this is a good strategy to use when it is not possible to investigate all age groups or by the researcher's own choice. Traumatic OMLs such as mucoceles and traumatic ulcers, and infectious, such as fistulae and herpetic infection, may be more frequent in children than in adults[14,31]. Similarly, denture and tobacco-related lesions, such as stomatitis, hyperplasia and leukoplakia affect adults more frequently[12]. These differences should be taken into account in the study design when defining the clinical diagnoses that will be investigated. In addition, it is important to note that not only differences in sex and age,

but also in race or ethnicity, tobacco and prosthesis use, for example, may also influence the pathologies prevalence. These factors must be taken into account when analyzing the results of the studies[12].

In relation to the exclusion of some diagnoses such as Fordyce granules, fissured and geographic tongue, exostosis, among others, which belong to a group known as developmental defects or variations in normality[3,31,40], it is important to consider the differences in the prevalence of OMLs that the decision to include or not include this group can lead to[4,32]. Because of the relatively common occurrence of these alterations, the overall prevalence of OMLs may be higher in certain populations if developmental alterations are included [1,24,25,31]. It is interesting to note that most of those require no treatment and have little relevance in terms of oral health[4], so one should think very carefully about the design of the study whether they will be included or not.

Similarly, the inclusion of transitory and recurrent oral conditions may increase the prevalence of OMLs in the studied populations. There are two ways of investigating the prevalence of transitory and recurrent oral conditions such as recurrent aphthous ulceration and herpetic infection: through clinical examination and through self-reported lifetime history. Kleinman et al.[38] and Reichart[29] investigated these pathological entities through these two forms in populations of American children. It is interesting to note that the two forms contain important biases due to the transitory and recurrent nature of the diseases and losses that can occur when considering the reporting done by the individuals, although the self-reported prevalence exceeds that verified by clinical examination[28,29,38]. One possibility would be observe individuals several times over a long period[16], but the best option may be to exclude these transitory and recurrent conditions in studies about the prevalence of OMLs, aiming for greater comparability between them and more reliable results.

In addition, it is important to emphasize the importance of using specific clinical diagnoses rather than to classify the conditions according only to the fundamental lesion. Three studies included in this review classified the pathologies in fundamental lesions. Besides the difficulty in comparing them with others in the literature, there is no detail about the condition that those lesions described as macula, plaque, papule/ nodule, vesicle/bubble, erosion or ulcer represent[2,4,5]. A papule or nodule, for example, may represent a reactive or infectious lesion; an erosion may represent a traumatic, allergic or infectious process and even a potentially malignant or malignant change[4]. Moreover, differences in OMLs prevalence can be observed depending on the grouping of lesions.

Usually, the groups present slight variations, like, for example, the inclusion of candidiasis in the denture-related lesions group[27] or in the infectious group[1] or in the group of red or white lesions[24,35], what implies in different prevalence outcomes.

Not only the prevalence of lesions is interesting to investigate but also the characteristics of these lesions[16]. This review showed that very few studies have performed this analysis[4,5,14]. Detailing data on size, color, consistency, surface appearance, associated symptoms and time of evolution are also important in order to know better how those lesions of higher prevalence presented to clinical examination, helping in the construction of differential diagnoses and in the establishment of the final diagnosis. Moreover, it is important to emphasize that the location of an oral lesion is often critical in determining its differential diagnosis[45]. In relation to the symptomatology that may be associated with the lesions, Correa et al.[4] included in their research specific questions about discomfort, pain, burning sensation and itching associated with the OMLs investigated.

Another relevant aspect is to encourage the adoption of examiners' training and calibration, so that the conditions should be viewed in a similar way as possible by the different individuals who perform the clinical exams[4,5]. In this review, only 15 (51.7%) studies accessed intra and/or inter-examiner agreement. It is recognized that this step is challenging because the same pathology may have different clinical presentations in distinct patients, the conditions can present different stages of manifestation, and the sites of occurrence may vary between individuals[16]. In fact, some lesions can be easily diagnosed by their clinical characteristics, such as mucoceles and fibrous hyperplasias, but others may require laboratory and/or histological tests to establish the final diagnosis, such as leukoplakia and pigmented lesions, being diagnosed clinically with less accuracy[14,16]. Moreover, the rarity and different clinical aspects of some oral conditions may interfere with the replication of the exams during calibration, and the process sometimes has to be done through the analysis of photographs[14]. These reasons may explain in part why few studies have calibrated examiners, despite the importance of this step. Additionally, for investigations of long duration, quality control procedures and recalibration are essential for monitoring[16].

Therefore, the standardization of the methodologies used in population-based studies on the prevalence of OMLs is extremely important. The shorter and more standardized the spectrum of references used in the methodology of studies, the easier it is to reproduce them and compare results from different populations[16,43,46]. However, the

results of this systematic review showed that the use of a standard methodology is uncommon (Table 1), although the great majority of the studies have used WHO criteria associated or not with those published by Tony Axéll and colleagues. The most current version of WHO to conduct studies of this type is the "Oral health surveys: basic methods - 5th edition (2013)"[46] which can be used in conjunction with "Guide to epidemiology and diagnosis of oral mucosal diseases and conditions (1980)"[43] also from WHO.

There are some limitations in observational studies such as the loss of information, difficulties related to the conditions that the exam is performed, such as participants´ home, and also those associated to clinical examination in terms of acceptance and availability of the patient[39]. They should be minimized as far as possible. MacEntee and colleagues[39] investigated why 51% of the individuals who were interviewed did not receive oral examination. They found that most of them (72%) believed that oral examination was not valid, 22% did not want to be inconvenienced and 6% were afraid of dentists. Reporting in the study the causes of non-response is important to analyze the losses and evaluated their implication in the results.

Even well-conducted population-based studies in terms of both sampling, design and conduction are valid for the country or region in which they were performed but may not produce valid estimates of prevalence in other countries, since risk factors for OMLs may vary around the world, in view of cultural and geographic differences[12,16]. In any case, this type of study has undeniable validity and should be strongly stimulated to be carried out in the most diverse areas of oral health, aiming more robust research results.

In general, we could evaluate population-based studies on OMLs prevalence in relation to methodological aspects such as sampling, design and conduction, including diagnostic criteria, examiner training and data collection. We concluded that there is a lack of standardization in some of these aspects, mainly related to unbiased evaluation, adequate reported response rate and presentation of results with respective confidence intervals. Therefore, we encourage that new researches in this field incorporate recognized references and applied standard methods, aiming to augment their quality, reliability, reproducibility, decrease bias and facilitate the comparisons between studies in future systematic reviews and meta-analysis in this important oral health topic.

ACKNOWLEDGEMENTS

KDS and WLOR are funded by Coordination for the Improvement of Higher Education Personnel (Capes – Brazil). JPAS is funded by Partnerships Program for

Education and Training (PAEC) between the Organization of American States (OAS) and the Coimbra Group of Brazilian Universities (GCUB), and RSO is funded in part by Meridional Foundation (Passo Fundo – Brazil) and in part by Capes.

REFERENCES

1. Feng J, Zhou Z, Shen X, et al. Prevalence and distribution of oral mucosal lesions: a cross-sectional study in Shanghai, China. *J Oral Pathol Med.* 2015;44:490-4.

2. Do LG, Spencer AJ, Dost F, Farah CS. Oral mucosal lesions: findings from the Australian National Survey of Adult Oral Health. *Aust Dent J*. 2014;59:114-20.

3) Sedano HO, Carreon Freyre I, de la Garza MLG, et al. Clinical orodental abnormalities in Mexican children. *Oral Surg Oral Med Oral Pathol.* 1989;68:300-11.

4) Tarquinio SBC, de Oliveira LJC, Correa MB, et al. Factors associated with prevalence of oral lesions and oral self-examination in young adults from a birth cohort in Southern Brazil. *Cad Saúde Pública*. 2013;29:155-164.

5) de Oliveira LJ, Torriani DD, Correa MB, et al. Oral mucosal lesions' impact on oral health-related quality of life in preschool children. *Community Dent Oral Epidemiol*. 2015;43:578-85.

6) Villanueva-Vilchis MC, López-Ríos P, García IM, Gaitán-Cepeda LA. Impact of oral mucosa lesions on the quality of life related to oral health. An etiopathogenic study. *Med Oral Patol Oral Cir Bucal*. 2016;21:e178-84.

7) Axéll, T. A preliminary report on prevalences of oral mucosal lesions in a Swedish population. *Community Dent Oral Epidemiol*. 1975;3:143-5.

8) Majorana A, Bardellini E, Flocchini P, Amadori F, Conti G, Campus G. Oral mucosal lesions in children from 0 to 12 years old: tem years' experience. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2010;110:e13-e18.

9) Sykara M, Ntovas P, Kalogirou EM, Tosios KI, Sklavounou A. Oral lymphoepithelial cyst: A clinicopathological study of 26 cases and review of the literature. *J Clin Exp Dent*. 2017;9:e1035-e1043.

10) Uchoa-Vasconcelos AC, Filizola-de Oliveira DJ, Roman-Martelli SJ, Etges A, Neutzling-Gomes AP, Chaves-Tarquínio SB. Demographic profile of oral nonodontogenic cysts in a Brazilian population. *Med Oral Patol Oral Cir Bucal.* 2014;19:e308-e312.

11) Castellanos JL, Díaz-Guzmán L. Lesions of the oral mucosa: an epidemiological study of 23785 Mexican patients. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2008;105:79-85.

12) Mendez M, Carrard VC, Haas AN, et al. A 10-year study of specimens submitted to oral pathology laboratory analysis: lesion occurrence and demographic features. *Braz Oral Res*. 2012;26:235-41.

13) Shulman JD, Beach MM, Rivera-Hidalgo F. The prevalence of oral mucosal lesions in U.S. adults: data from the Third National Health and Nutrition Examination Survey, 1988-1994. *J Am Dent Assoc*. 2004;135:1279-86.

14) Shulman JD. Prevalence of oral mucosal lesions in children and youths in the USA. *Int J Paediatr Dent*. 2005;15:89-97.

15) Chung CH, Yang YH, Wang TY, Shieh TY, Warnakulasuriya S. Oral precancerous disorders associated with areca quid chewing, smoking, and alcohol drinking in southern Taiwan. *J Oral Pathol Med*. 2005;34:460-6.

16) Kleinman DV, Swango PA, Niessen LC. Epidemiologic studies of oral mucosal conditions - methodologic issues. *Community Dent Oral Epidemiol*. 1991;19:129-40.

17) Carrard V, Haas A, Rados P, et al. Prevalence and risk indicators of oral mucosal lesions in an urban population from South Brazil. *Oral Dis*. 2011;17:171-9.

18) Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol*. 2009;62:1006-12.

19) Loney PL, Chambers LW, Bennett KJ, Roberts JG, Stratford PW. Critical appraisal of the health research literature: prevalence or incidence of a health problem. *Chronic Dis Can*. 1998;19:170-176.

20) Kassebaum NJ, Bernabé E, Dahiya M, Bhandari B, Murray CJ, Marcenes W. Global burden of severe periodontitis in 1990-2010: a systematic review and meta-regression. *J Dent Res*. 2014;93:1045-53.

21) Witkop, CJ, Barros L. Oral and Genetic Studies of Chileans 1960. I Oral anomalies. *Am J Phys Anthropol.* 1963;21:15-24.

22) Campisi G, Margiotta V. Oral mucosal lesions and risk habits among men in an Italian study population. *J Oral Pathol Med*. 2001;30:22-8.

23) Espinoza I, Rojas R, Aranda W, Gamonal J. Prevalence of oral mucosal lesions in elderly people in Santiago, Chile. *J Oral Pathol Med*. 2003;32:571-5.

24) Ghanaei FM, Joukar F, Rabiei M, Dadashzadeh A, Valeshabad AK. Prevalence of Oral Mucosal Lesions in an Adult Iranian Population. *Iran Red Crescent Med J*. 2013;15: 600-604.

25) Jahanbani J, Morse DE, Alinejad H. Prevalence of oral lesions and normal variants of the oral mucosa in 12 to 15-year-old students in Tehran, Iran. *Arch Iran Med*. 2012;15:142-5.

26) Lin HC, Corbet EF, Lo EC. Oral mucosal lesions in adult Chinese. *J Dent Res*. 2001;80:1486-90.

27) Mumcu G, Cimilli H, Sur H, Hayran O, Atalay T. Prevalence and distribution of oral lesions: a cross-sectional study in Turkey. *Oral Dis*. 2005;11:81-7.

28) Parlak AH, Koybasi S, Yavuz T, et al. Prevalence of oral lesions in 13- to 16-year-old students in Duzce, Turkey. *Oral Dis*. 2006;12:553-8.

29) Reichart, PA. Oral mucosal lesions in a representative cross-sectional study of aging Germans. *Community Dent Oral Epidemiol*. 2000;28:390-8.

30) Splieth CH, Sümnig W, Bessel F, John U, Kocher T. Prevalence of oral mucosal lesions in a representative population. *Quintessence Int*. 2007;38:23-9.

31) Vieira-Andrade RG, Martins-Júnior PA, Corrêa-Faria P, et al. Oral mucosal conditions in preschool children of low socioeconomic status: prevalence and determinant factors. *Eur J Pediatr*. 2013;172:675-81.

32) Corbet EF, Holmgren CJ, Philipsen HP. Oral mucosal lesions in 65-74-year-old Hong Kong Chinese. *Community Dent Oral Epidemiol*. 1994;22:392-5.

33) Zain RB, Ikeda N, Razak IA, et al. A national epidemiological survey of oral mucosal lesions in Malaysia. *Community Dent Oral Epidemiol*. 1997;25:377-83.

34) Bánóczy J, Rigó O. Prevalence study of oral precancerous lesions within a complex screening system in Hungary. *Community Dent Oral Epidemiol*. 1991;19:265-7.

35) Osterberg T, Ohman AL, Heyden G, Svanborg A. The condition of the oral mucosa at age 70: a population study. *Gerodontology*. 1985;4:71-5.

36) Salonen L, Axéll T, Helldén L.J. Occurrence of oral mucosal lesions, the influence of tobacco habits and an estimate of treatment time in an adult Swedish population. *Oral Pathol Med*. 1990;19:170-6.

37) Sedano HO. Congenital oral anomalies in argentinian children. *Community Dent Oral Epidemiol*. 1975;3:61-3.

38) Kleinman DV, Swango PA, Pindborg JJ. Epidemiology of oral mucosal lesions in United States schoolchildren: 1986-87. *Community Dent Oral Epidemiol*. 1994;22:243-53.

39) MacEntee MI1, Glick N, Stolar E. Age, gender, dentures and oral mucosal disorders. *Oral Dis*. 1998;4:32-6.

40) Sawyer DR, Taiwo EO, Mosadomi A. Oral anomalies in Nigerian children. *Community Dent Oral Epidemiol*. 1984;12:269-73.

41) Sawyer SM, Azzopardi PS, Wickremarathne D, Patton GC. The age of adolescence. *Lancet Child Adolesc Health*. 2018;2:223-228.

42) Roed-Petersen B, Renstrup G. A topographical classification of the oral mucosa suitable for electronic data processing. Its application to 560 leukoplakias. *Acta Odontol Scand*. 1969;27:681-95.

43) Kramer IR, Pindborg JJ, Bezroukov V, Infirri JS. Guide to epidemiology and diagnosis of oral mucosal diseases and conditions. World Health Organization. *Community Dent Oral Epidemiol*. 1980;8:1-26.

44) PELOTAS (BRAZIL) BIRTH COHORTS. Disponível em: <http://www.epidemio-ufpel.org.br/site/content/estudos/index.php>. Acesso em 08 abr. 2018.

45) Bouquot JE. Common oral lesions found during a mass screening examination. *J Am Dent Assoc*. 1986;112:50-7.

46) World Health Organization (WHO). Oral health surveys: basic methods. WHO: Geneva; 1980. 4th edn. 125p.

Table 1. Demographic data and methodological aspects of included studies.

Author and country	Sample size (n)[1] and subjects	Other data collected[2]	References adopted[3]	OML[4] type (groups)
Bánóczy & Rigó (1991) *Hungary*	7820 All age groups and sex	Alcohol and tobacco consumption, denture wearing and subjective complaints	Previous studies of the author+Axéll (1984)+ Roed-Petersen & Renstrup (1969)	Precancerous (Leukoplakia and lichen planus)
Campisi & Margiotta (2001) *Italy*	118 Only men >40 years	Occupation, alcohol and tobacco consumption, knowledge of the correlation between oral and general health and the deleterious effects of tobacco and alcohol to oral mucosa, use of mouthrinses and oral hygiene condition	WHO (1980)+ Axéll (1996)+Scully (1993)	All (not grouped)
Carrard et al. (2011) *Brazil*	1586 Both sex ≥14 years	Socioeconomic status, smoking and alcohol consumption, use of prosthesis, oral hygiene habits and periodontal condition.	WHO (1980)+WHO (1997)	All (Premalignant lesions, proliferative lesions, abscess and fistulas and oral candidiasis)
Chung et al. (2005) *Taiwan*	1075 Both sex ≥15 years	Education, smoking, alcohol and areca quid consumption, diabetes or hypertension diseases	WHO (1978, 1980) + Axell (1996)	Precancerous (not grouped)
Corbet et al. (1994) *Hong Kong*	537 Both sex Between 65-74 years	Smoking and alcohol consumption, denture wearing	WHO (1980) + Axéll (year not informed) + a color atlas prepared by one of the authors	All (not grouped)
Do et al. (2014) *Australia*	5505 Both sex ≥15 years	Socioeconomic level, eligibility for public dental care, rural or urban residence, health-related factors, smoking consumption	WHO (1977) + Slade (2007)	All (No mucosal pathology, suspected malignancy, ulceration, all other non-ulcerated OMLs[4])
Espinoza et al. (2003) *Chile*	889 Both sex >65 years	Educational level, use of the public health system, visit to the dentist, denture status, smoking associated variables, medication use, sistemic diseases, xerostomia	WHO (1980, 1997)+Axéll (1976, 1996)	All (not grouped)
Feng et al. (2015) Shangay	11054 All age groups and sex	Smoking and alcohol comsumption	Do (2014) + WHO (1978, 1997)	All (Tongue lesions, ulcers, infections, witish lesion, melanin pigmentation, tumor/tumor-like lesion, xerostomia/burning mouth syndrome, pemphigus, others)
Ghanaei et al. (2013) *Iran*	1581 Both sex >30 years	Smoking and opium comsumption, medication use, family history of oral	WHO (year not informed)	All (White color lesions and nonwhite lesions)

		câncer, oral and dental hygiene		
Jahanbani et al. (2012) *Iran*	1020 Both sex Between 12-15 years	-	WHO (1980)	All (not grouped)
Kleinman et al. (1994) *USA*	39206 Both sex Between 5-17 years	Race, region of origin, history of recurrent herpes labialis or recurrent aphthous ulcers, smoking and alcohol comsumption	Pindborg (1985) + Axéll (1976a, 1976b) + Greer (1985) + WHO (1977, 1980) + Roed-Petersen and Renstrup (1969)	All (not grouped)
Lin et al. (2001) *China*	3088 Both sex Between 35-44 and 65-74 years	Smoking and alcohol comsumption	WHO (1997) + Axéll (1976, 1984) + atlas prepared by the authors	All (Precancerous lesion and condition, other white lesion, ulcers, lesions related to infection, tongue lesions, tumor, excessive melanin pigmentation, others)
MacEntee et al. (1998) *Canada*	255 Both sex ≥70 years	Occupation, income, education, self-perceived oral health, use of dental service, denture wearing	Axéll (1976)	All (not grouped)
Muncu et al. (2005) Turkey	765 All age groups and sex	Smoking comsumption, medical and oral health history, medications, denture wearing and denture cleaning habits	WHO (1980, 1997) + Scully (1999)	All (Pigmentation, tongue lesions, denture-related lesions, red mucosal lesions, tumors, white mucosal lesions, recurrent aphtous stomatitis, hypertrophic frenulum, salivary gland diseases, infections, others)
Oliveira et al. (2015) *Brazil*	1118 Both sex 5 years-old children	Family income and maternal schooling at children's birth, caries, malocclusion and oral health related quality of life of children	WHO (1987)	All (Ulcer, papule/nodule, pigmented lesion, erosion, vesicles/blisters, white plaques, indefinite)
Osterberg et al. (1985) *Sweden*	385 Both sex 70 years-old adults	Marital situation, education, family income, smoking comsumption, medication use, sistemic diseases, dental and denture situations	Roed-Pedersen & Renstrup (1969)	All (Red, white and hyperplastic lesions, and tongue lesions)
Parlak et al. (2006) *Turkey*	993 Both sex Between 13-16 years	*Venous blood samples were obtained for detecting hemoglobin levels	WHO (1980)	All (not grouped)
Reichart (2000) *Germany*	2022 Both sex Between 35-44	Educational level, subjective oral health, visits to the dentist, use of worn dentures, denture made in the current year, history of recurrent	WHO (1980) + Melnick (1993) + Ramanathan (1995) + Axéll (1976) + Zain (1995) + WHO (1995) + Roed-Petersen &	All (not grouped)

	and 65-74 years	aphthous ulceration or herpetic infections	Renstrup (1969) + manual prepared by the authors	
Salonen et al. (1990) *Sweden*	920 Both sex ≥20 years	Cigarette, pipe smoking or snuff dipping consumption, denture wearing	Axéll (1976, 1984, 1987) + WHO (1978) + Roed-Petersen & Renstrup (1969)	All (Infections, ulcers, witish lesions, denture related lesions, tongue lesions, pigmentation, tumor and tumor-like lesions)
Sawyer et al. (1984) *Nigeria*	2203 Both sex Between 10-19 years	Ethnicity	-	Oral anomalies (not grouped)
Sedano (1975) *Argentina*	6180 Both sex Between 6-15 years	-	-	Orodental abnormalities (not grouped)
Sedano et al. (1989) *Mexico*	32022 Both sex Between 5-14 years	-	-	Congenital oral anomalies (not grouped)
Shulman et al. (2004) *USA*	17235 Both sex ≥17 years	Race/ethnicity, smoking comsumption, denture wearing	WHO (1980) + NHANES III (1992)	All (Candida related, tobacco-related, acute conditions, tongue conditions, red/white conditions, raised conditions, other conditions)
Shulman (2005) *USA*	10032 Both sex Between 2-17 years	Race-ethnicity	WHO (1980) + NHANES III (1992)	All (Candida related, tobacco-related, acute conditions, tongue conditions, red/white conditions, raised conditions, other conditions)
Splieth et al. (2007) Germany	4210 Both sex Between 20-79 years	-	Reichart (1993) + Roed-Petersen & Renstrup (1969)	All (Leukoplakia simplex, leukoplakia verrucosa, leukoplakia erosive, erythroplakia, lichen ruber, ulcer of the oral mucosa, exophytic neoplasia, herpetiform lesion or aphthous lesion, not classifiable, suspicious change of oral mucosa)
Tarquinio et al. (2013) *Brazil*	720 Both sex 24-years-old adults	Skin color, maternal schooling and family income at birth, smoking at age 22, oral self-examination, oral hygiene instruction from a dentist up to the age of 15 years	Hipólito & Martins (2010) + Neville (2009)	All (Pigmented lesions, papules and nodules, white plaque, vesicles and bubbles, erosion, ulcer)

Vieira-Andrade et al. (2013) *Brazil*	541 Both sex Between 0-5 years	Residence of the child, mother's schooling, monthly household income, decayed, missing and filled teeth, oral hygiene level., presence of harmful oral habits of the child and bruxism	Bessa (2004) + WHO (1995, 1997)	All (not grouped)
Wiktop & Barros (1963) *Chile*	1906 All age groups and sex	*A blood sample was obtained for vitamin assay, genotyping and other laboratory determinations	-	Oral anomalies (not grouped)
Zain et al. (1997) *Malaysia*	11697 Both sex ≥25 years	Ethnicity	WHO (1978, 1980) + Axéll (1976, 1984) + Zain (1996) + Reichart (1987) + Ikeda (1995)	All (not grouped)

- Data not reported
1 Patients from whom data on oral mucosal lesions were obtained
2 Important data collected other than on oral mucosal lesions
3 References used to conduct the study, in terms of examiner training and data collection. The full references are shown as Appendix C.
4 OML: oral mucosal lesions

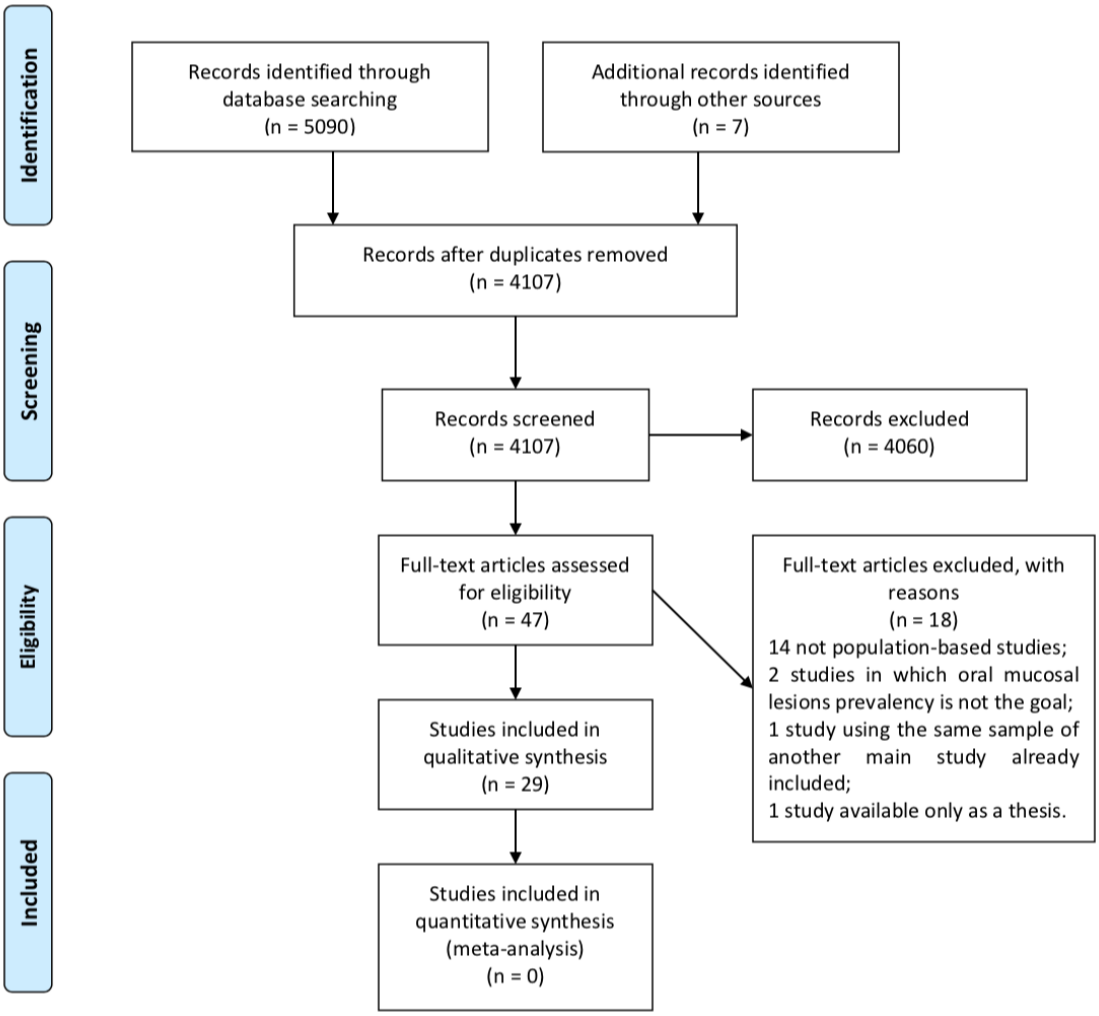


Fig. 1. Search flow according to the Prisma Statement.

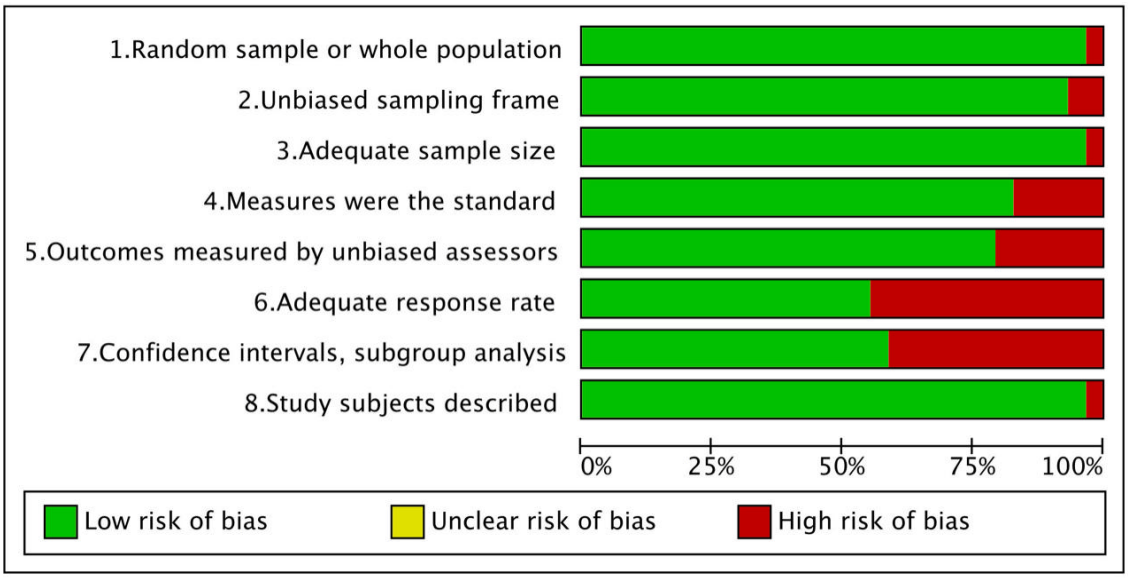


Fig. 2. Review authors' judgements about each risk of bias item presented as percentages across all included studies, according to Loney et al.[19].

3 Capítulo 2

Oral mucosal lesions in pregnants: A population-based study

Karine Silva[a*], Fernando Barros[b], Flávio Demarco[c], Marcos Correa[d], Sandra Tarquinio[c]

Running title: Oral mucosal lesions in pregnants

[a] Post Graduate student, School of Dentistry, Federal University of Pelotas, Pelotas-RS, Brazil

[b] Adjunct professor, School of Medicine, Universidade Católica de Pelotas, Pelotas-RS, Brazil

[c] Titular professor, School of Dentistry, Federal University of Pelotas, Pelotas-RS, Brazil

[d] Adjunct professor, School of Dentistry, Federal University of Pelotas, Pelotas-RS, Brazil

*Corresponding author:

Karine Duarte da Silva

Address: Gonçalves Chaves Street, 457, Pelotas-RS, Brazil, Zip Code 96015-560

Telephone and Fax number: +55 53 32256741 (extension 162)

Email address: karineduartedasilva1@gmail.com

O artigo será submetido ao periódico *Medicina Oral Patologia Oral y Cirugia Bucal* (Qualis B1; Fator de Impacto: 1.671) e está formatado segundo as normas da revista.

Abstract

Objectives: To evaluate the prevalence of oral mucosal lesions in pregnant mothers belonging to the 2015 birth cohort of Pelotas (Brazil).

Study design: Population-based cross-sectional study conducted among pregnant women living in the urban area of Pelotas and with delivery estimated in the year 2015. Questionnaires and clinical exams were applied. Oral mucosal lesions (OMLs) were investigated, among other oral health conditions. Nineteen clinical diagnoses were included and grouped in six categories. Size, location, duration referred and associated symptoms of the lesions were also collected, in addition to sociodemographic, behavioral variables, and dental history. Data were analyzed descriptively.

Results: Data from 2481 pregnants were useful to analysis. Four hundred and nine (16.49%) individuals have at least one OML, being 482 the total of lesions. The most frequent clinical diagnosis were exostosis (79 -16.39%), coated tongue (70-14.52%), and benign oral brownish pigmentation (65-13.49%). The most prevalent groups were developmental alterations (262-54.35%), benign oral brownish pigmentation (68-14.11%), and infectious diseases (67-13.90%). A hundred and ten (8.22%) pregnant women were current smokers. Almost 50% of respondents have never performed oral self-examination. Relating to dental history, more than 86% of mothers informed that they received no orientation about oral health during pregnancy.

Conclusion: It was found a relatively small number of OMLs in this population. Pregnant women had not yet been investigated about OMLs prevalence, thus the data may be valid to oral health promotion and information of these mothers.

Key words: prevalence, pregnant women, mouth diseases, oral health, Brazil

INTRODUCTION

The spectrum of oral mucosal lesions (OMLs) in different population groups can be variable, including since indolent conditions such as fibrous hyperplasias, pyogenic granulomas, and mucoceles, until rare pathological alterations with a more agressive clinical course and poor prognosis, such as neoplasms like squamous cell carcinoma, sarcomas, and metastatic lesions (1-3). Although they may cause important aesthetic and functional changes, OMLs are often neglected in clinical exams and epidemiological studies (2,4).

Most epidemiological studies involving OMLs were conducted in outpatient services or in histopathological analysis laboratories (5,6), with few population-based investigations performed on this topic (1,2,7,8), which makes difficult to know the real prevalence of these conditions in the general population. In addition, the knowledge of the prevalence of these lesions in specific population groups is important, such as pregnants, in order to promote interventions aimed at clarifying and preventing these conditions. However, none population-based study so far has investigated the prevalence of OMLs in pregnants.

Pregnant women present biological and behavioral changes characteristic of the gestational period, which may predispose them to the development not only of caries and periodontitis, as reported in the literature (9,10), but also some OMLs (11,12). Hormonal changes, such as high levels of estrogen and progesterone, are capable to augment the inflammation levels and predispose to the development of OMLs in these women (9,11,12). One example is pyogenic granuloma, a benign pathology that usually occurs in the gingiva and is a result of exaggerated inflammatory response to local irritations such as trauma or dental plaque accumulation (11,12).

Moreover, socio-demographic issues such as schooling and income may also be related to the development of oral lesions, as well as aspects related to the dental history, such as the last visit to the dentist, the orientations on oral hygiene, flossing and bleeding on brushing (7,13). These aspects may be implicated not only in oral health of pregnant women, but also in health conditions of their children (9,14). Therefore, knowing the prevalence of OMLs in pregnants is a first step in the promotion of this women's oral health.

The present study aims to evaluate the prevalence of OMLs in pregnant mothers of the individuals belonging to the birth cohort of Pelotas (Brazil) in 2015.

METHODOLOGY

Study design

A population-based study was conducted among pregnant women living in the urban area of Pelotas, a medium-sized city located in the state of Rio Grande do Sul, with approximately 345,000 inhabitants in 2017 (15). Historically, several birth cohort studies have been conducted in Pelotas (16), being the Pelotas Birth Cohort Study of 2015 (17) a large population-based study that, in addition to evaluating all children born in the city in 2015, evaluated the mothers of these individuals during the gestational period. In the prenatal study, pregnant women who lived in the urban area of Pelotas and who had a scheduled delivery date between 15 December 2014 and 19 May 2016 were recruited. Recruitment took place from all health facilities that offered prenatal care (public and private),

including clinical laboratories, ultrasound clinics, basic health units, hospitals, clinics/polyclinics, universities and private practices. Details on the design of this cohort can be found in a previous study (22).

The interviews were conducted respecting the availability of each pregnant, so some of them occurred at the home of individuals or their relatives and others at the Epidemiological Research Center of the Federal University of Pelotas. Three types of questionnaires were administered according to gestational age at the time of inclusion in the study: (1) women recruited before the 16th week of pregnancy responded to the initial assessment questionnaire that included socioeconomic and demographic data; (2) for women responding to the first questionnaire, a major evaluation questionnaire was administered between weeks 16 and 24 of gestation; and (3) women who were screened after 16 weeks and up to 24 weeks of pregnancy responded to a questionnaire that consisted of a combination of the information collected in the initial assessment and the main assessment. The questionnaires can be found at http://www.epidemio-ufpel.org.br/site/content/coorte_2015/questionarios.php. A total of 3199 pregnant women investigated gave birth to individuals who actually participated in the 2015 Cohort.

Eligible pregnants for the oral health study were those who were between 16 and 24 weeks of gestation. Oral exams were conducted after the interview by one of 15 trained and calibrated examiners and one trained interviewer. The training and calibration process was conducted by an experienced oral pathologist (gold standard) through a theoretical lecture followed by calibration *in lux* (projection of images). The inter-examiner agreement was measured by the Kappa statistic, with a lower value of 0.88 for OMLs. The pregnant women were examined under artificial headlights by examiners who were adequately identified as members of the study and adopted adequate biological risk barriers. Before the examination, the mucosa was dried with gauze. Wooden spatulas and mouth mirrors were used. Several dental health conditions were investigated, such as dental crown conditions, periodontal diseases, use and need of prosthesis, evaluation of restorations, occlusion, dental wear and OMLs.

The prenatal study was approved by the Ethics Committee of the Faculty of Medicine of the Federal University of Pelotas (protocol number 717.271/2014) (Annex A).

Outcomes

The investigated outcome (dependent variable) was OML, which was dichotomized in yes and no. Throughout this study OMLs refer to lesions of the oral mucosa excluding periodontitis. The 19 clinical diagnoses included in the research were based on a World Health Organization guide (18). The lesions were grouped for analysis in 6 groups, according to a previous work adaptation (19), as follows:

1) White and red: leukoplakia and erythroplakia
2) Infectious: secondary herpetic infection, buccal candidiasis, mucosal lesions due to pulpal or periodontal infections (parulis), and necrotizing ulcerative gingivitis
3) Swellings: reactive gingival lesions and fibroma
4) Ulcers: recurrent aphthous ulceration, traumatic ulcer

5) Benign oral brownish pigmentation
6) Developmental alterations: Fordyce granules, geographic tongue, fissured tongue, coated tongue, varicosities and exostoses (mandibular and palatine torus, and vestibular exostoses)

Still in relation to OMLs, were investigated: location (17 specific sites grouped into lip, vestibule and gums, buccal mucosa and labial commissure, hard palate, soft palate and tonsillar pillar, tongue, and floor of the mouth), size (≤5mm, between 6-10mm, 11-20mm, ≥21mm, and multiple lesions not measured), duration referred (no/never noticed the lesion, observed for less than 1 month, between 1-6 months, 6 months-1 year,> 1 year) and associated symptoms (pain, burning, itching and discomfort, dichotomized in yes and no).

Co-Variables

Socioeconomic, demographic, behavioral variables and dental history were also collected. These independent variables included sociodemographic aspects such as maternal age (categorized as adolescent, ≤20 years; young adult, 21-39 years; and adult, ≥40 years), skin color (white, black, yellow, brown/indigenous), and schooling (in complete years, 0-4, 5-8, 9-11, 12 or more), income (quintiles); habits such as tobacco use (yes/no, in addition to consumed amount of tobacco) and oral self-examination (never, always, sometimes); and dental history which included flossing (no/never, yes/sometimes, yes/almost always), bleeding on brushing (no, yes/sometimes, yes/almost always), going to the dentist in the last month (yes/no), and orientations on oral hygiene during pregnancy by a professional (yes/no).

Data analysis

The software Stata version 12.0 (Stata Corp., College Station, USA) was used for the analysis. Descriptive analysis was performed to determine the relative and absolute frequencies of the variables of interest.

Ethical considerations

All participants gave written and informed consent prior to the interview and oral examination (Appendix D) . For eligible participants under the age of 15, written consent to participate in the study was obtained from their parents or guardians.

Those pregnant women who presented oral lesions and asked about dental treatment were instructed to seek the Faculty of Dentistry of the Federal University of Pelotas and the Center for Diagnosis of Oral Diseases of the same institution. A folder of the center was made available for easy contact.

RESULTS

In the oral health study performed with the pregnant mothers of the individuals belonging to the 2015 birth cohort, 3125 women were eligible, of which 25 (0.8%) refused to participate. Thus, valid oral health data were obtained for 2481 (80.03%), since mothers who had stillborn children, did not complete

gestation, and had a delivery outside the period of interest were excluded from the prenatal study.

Table 1 shows the sociodemographic characteristics of the pregnants and their oral health habits. Most of them were young adults, with white skin color, at least 9 years of schooling and they was well distributed among the 5 income quintiles. Related to oral habits, flossing, bleeding on brushing and visit to the dentist in last month presented favorable results, only orientation on oral hygiene by a professional could be improved.

Regarding tobacco consumption, 110 (8.22%) pregnant women reported being current consumers, with 81 (73.63%) of them referring to be light consumers (1-10 cigarettes/day). In addition, almost 50% of respondents claimed to have never performed oral self-examination, 1169 (47.12%). Another 435 (17.53%) said always perform it, and 877 (35.35%) sometimes.

The number of pregnant women with at least one OML was 409, representing 16.49% of the study population. A total of 482 lesions were found in these mothers, with 64 (15.88%) of them presenting 2 lesions at the time of the examination, and 9 (2.23%) having 3 alterations. The most frequent clinical diagnosis were exostosis, 79 (16.39%), coated tongue, 70 (14.52%), and benign oral brownish pigmentation, 65 (13.49%). The lesions prevalence according to groups, as well as their characteristics can be seen in Table 2. Developmental alterations and benign oral brownish pigmentation were the groups that presented the highest prevalences, followed by the infectious group. The last was represented mainly by mucosal lesions resulting from pulpal or periodontal bacterian infections (parulides), responsible for 44 (9.13%) of the oral lesions found.

DISCUSSION

The 2015 Pelotas Cohort has provided important information on aspects related to maternal and child health. The prenatal study involved 73.8% of the mothers who subsequently gave birth to the children included in the cohort (17). In the oral health study, 2481 pregnant women were evaluated, providing data on diverse oral conditions, such as caries and periodontitis, as well as OMLs. A similar study was conducted in two other Brazilian cities, but despite of evaluating pregnant women, it did not collect data on OMLs (10). In fact, this aspect of oral health is still little investigated in epidemiological studies, mainly in population-based ones (2,7,8,20). Comparing OMLs prevalence between service-based and population-based studies, it can be observed a higher prevalence in the first, which is closely related to the selection bias inherent to those studies (5,21).

This is the first population-based study that evaluated OMLs in pregnant women, revealing a OMLs prevalence of 16.49%. This value is higher than the 10.8% prevalence reported by Feng et al. (2), but is smaller than 19.4% (22), 23.3% (7) and 27.9% (23) reported in previous population-based studies with adult individuals. Differences in these prevalences may be due to the different diagnoses included. Still in relation to the general prevalence of OMLs, it is interesting to observe which lesions were the main responsible for this value. In this study, exostoses, coated tongue and benign oral brownish pigmentation were the most prevalent alterations. Exostoses and coated tongue were included in the "developmental alterations" group, making more than 50% of the OMLs belonged to this group, which is favorable since it comprises lesions without notorious

clinical relevance. However, Kleinman et al. (24) highlight the importance of investigate OMLs prevalence by specific clinical diagnoses and not as a whole, since indolent conditions could be responsible for a high overall OMLs prevalence, and more worrying lesions could represent only a small number. In this study, as expected, we could observe this fact. Erythroplakias and leukoplakias, included in the group "white and red" lesions, represented only 1.87% of the lesions found.

Regarding the low prevalence of potentially malignant lesions such as erythroplakia and leukoplakia and the non-occurrence of oral cancer in the investigated population, the findings of the present study are in accordance with the literature for individuals in this age group. Potentially malignant and malignant lesions usually affect individuals over 40 years-old and are closely related to chronic smoking habit (25). In this study, only 8.22% of the pregnant women were smokers. As the risk of tobacco causing cancer is cumulative through the time, these individuals can develop such lesions later in life and the knowledge about the determinants of consumption, aiming to interrupt the habit, is important during the gestational period (26).

The pregnant women represent a group with distinct characteristics from the general population, not just related to biological aspects inherent to their condition (9,12), as well as due to the psychological and behavioral aspects associated with the pregnancy. Caries, periodontal disease and reactive gingival lesions such as pyogenic granuloma have been observed in pregnant women, mainly associated to the hormonal changes that occur in the period and lead to expressive gingival inflammation in the presence of dental plaque, calculus or trauma (9,11,27). However, in this study, only 8 (1.66%) cases of reactive gingival lesions (mainly represented by pyogenic granuloma) were found, which is a favorable finding and may be related to the relatively satisfactory dental history related by this population. It is interesting to observe that even in a population-based study conducted with 2481 pregnants, only 8 had pyogenic granuloma, a finding contradictory to the literature that has historically reported this lesion to be frequent in pregnant women (11,12,27).

The groups of lesions that presented the highest prevalence were "developmental alterations", followed by "benign oral brownish pigmentation" and "infectious" in descending order. The first one includes alterations that are not true pathologies, but variations of the normality of the oral and maxillofacial region, such as Fordyce granules, coated tongue, and exostoses (2,7). Exostoses and coated tongue were the most prevalent developmental alterations, representing 16.39% and 14.52%, respectively, of the lesions found. Although these variations have little relevance in terms of oral clinical implications and do not require treatment in the majority of cases (7), they were included in this study following the example of several other investigations on the subject (2,21,28). Although its inclusion may have overestimated the OMLs prevalence in pregnant women, it was possible to know the distribution of developmental alterations in this population group, which has been not yet investigated in relation to oral mucosal conditions.

Lesions occurred preferentially on the vestibule and gums, followed by tongue, and buccal mucosa or labial commissure. In more than 50% of cases the lesion size was identified as "multiple lesions not measured", a fact that may be

related to a considerable prevalence of coated tongue and benign oral brownish pigmentation which may present as multiple brownish macules due to melanin pigmentation mainly in darker-skinned individuals (29), remembering that 27.35% of the pregnant women investigated were black or brown. Regarding the duration of the lesions referred by the pregnant and the presence of symptoms, the data are consistent with the occurrence of lesions that are mostly painless, such as benign oral brownish pigmentation, or that cause only some discomfort, such as coated tongue, being therefore, or not perceived, either noticed for a long time without causing concerns in the individual (29).

In relation to the oral habits of pregnant women, such as flossing and bleeding on brushing, it was observed a good oral health in the majority of them. Considering the visits to the dentist in the last month, and about receiving oral hygiene guidance during pregnancy, more than 60% of pregnant women said they went to the dentist during the gestational period, but only 13.51% received guidance on how to take care of their oral health. Therefore, it is important to highlight the role of oral care orientations on the habits of the individuals, which may include oral self-examination and search for care, diagnosis and treatment (7,30).

As limitations, it was observed loss of information in some variables, unfortunately a frequent finding in epidemiological studies (1,7,8). As strengths, it is interesting to report the high response rate to oral exams, although there were some refusals that were not reversed. They may have occurred due to lack of time, lack of interest, fear of the dentist, or embarrassment regarding the oral condition (25). Additionally, the inter-examiner agreement was satisfactory, with the training and calibration process of the interviewers and examiners according to what is recommended by similar studies (7,8,24).

Although the number of pregnant women who presented some OML was relatively low, investigating this population is important in order to know the most prevalent OMLs, and to act in the promotion of oral health, providing knowledge to specific populations about oral conditions and how to take care of their mouth appropriately.

ACKNOWLEDGMENTS

This article is based on data from the study "Pelotas Birth Cohort, 2015" conducted by Postgraduate Program in Epidemiology at Universidade Federal de Pelotas, with the collaboration of the Brazilian Public Health Association (ABRASCO). The 2015 Pelotas (Brazil) Birth Cohort is funded by the Wellcome Trust (095582). Funding for specific follow-up visits was also received from the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (FAPERGS).

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

REFERENCES

1) Carrard V, Haas A, Rados P, Filho M, Oppermann R, Albandar J, et al. Prevalence and risk indicators of oral mucosal lesions in an urban population from South Brazil. Oral Dis. 2011;17:171-9.

2) Feng J, Zhou Z, Shen X, Wang Y, Shi L, Wang Y, et al. Prevalence and distribution of oral mucosal lesions: a cross-sectional study in Shanghai, China. J Oral Pathol Med. 2015;44:490-4.

3) Servato JP, de Paulo LF, de Faria PR, Cardoso SV, Loyola AM. Metastatic tumours to the head and neck: retrospective analysis from a Brazilian tertiary referral centre. Int J Oral Maxillofac Surg. 2013;42:1391–6.

4) Villanueva-Vilchis MC, López-Ríos P, García IM, Gaitán-Cepeda LA. Impact of oral mucosa lesions on the quality of life related to oral health. An etiopathogenic study. Med Oral Patol Oral Cir Bucal. 2016;21:178-84.

5) Majorana A, Bardellini E, Flocchini P, Amadori F, Conti G, Campus G. Oral mucosal lesions in children from 0 to 12 years old: tem years' experience. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010;110:13-18.

6) Mendez M, Carrard VC, Haas AN, Lauxen Ida S, Barbachan JJ, Rados PV, et al. A 10-year study of specimens submitted to oral pathology laboratory analysis: lesion occurrence and demographic features. Braz Oral Res. 2012;26:235-41.

7) Tarquinio SBC, de Oliveira LJC, Correa MB, Peres MA, Peres KG, Gigante DP, et al. Factors associated with prevalence of oral lesions and oral self-examination in young adults from a birth cohort in Southern Brazil. Cad Saude Publica. 2013;29:155-164.

8) de Oliveira LJ, 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. Community Dent Oral Epidemiol. 2015;43:578-85.

9) Figuero E, Carrillo-de-Albornoz A, Marin C, Tobias A, Herrera D. Effect of pregnancy on gingival inflammation in systematically healthy women: a systematic review. J Clin Periodontol. 2013;40:457–73.

10) Thomaz, ÉBAF et al. Desfechos perinatais e alterações na cavidade bucal: coortes brasileiras de Ribeirão Preto e São Luís. Rev. bras. epidemiol. 2015;18: 966-970.

11) Cardoso JA, Spanemberg JC, Cherubini K, Figueiredo MA, Salum FG. Oral granuloma gravidarum: a retrospective study of 41 cases in Southern Brazil. J Appl Oral Sci. 2013;21:215-8.

12) Ramos-e-Silva M, Martins NR. Oral and Genital Changes in Pregnancy, Clin Dermatol. 2016.

13) Barros MBA, Lima MG, Medina LPB, Szwarcwald CL, Malta DC. Social inequalities in health behaviors among Brazilian adults: National Health Survey, 2013. Int J Equity Health. 2016;15:148.

14) Middleton P, Esposito M, Iheozor-Ejiofor Z. Treating periodontal disease for preventing adverse birth outcomes in pregnant women. Cochrane Database Syst Rev. 2017;6:12.

15) Instituto Brasileiro de Geografia e Estatística. From: https://www.ibge.gov.br/index.php. Retrieved: 07.05.2018.

16) Barros AJD, Santos ISS, Matijasevich A, Araújo CL, Gigante DP, Menezes AMB, et al. Methods used in the 1982, 1993, and 2004 birth cohort studies from Pelotas, Rio Grande do Sul State, Brazil, and a description of the socioeconomic conditions of participants' families. Cad. Saude Publica. 2008;3:371-380.

17) Hallal PC, Bertoldi AD, Domingues MR, Silveira MFD, Demarco FF, da Silva ICM, et al. Cohort Profile: The 2015 Pelotas (Brazil) Birth Cohort Study. Int J Epidemiol. 2017.

18) Kramer IR, Pindborg JJ, Bezroukov V, Infirri JS. Guide to epidemiology and diagnosis of oral mucosal diseases and conditions. World Health Organization. Community Dent Oral Epidemiol. 1980;8:1-26.

19) dos Santos PJ, Bessa CF, de Aguiar MC, do Carmo MA. Cross-sectional study of oral mucosal conditions among a central Amazonian Indian community, Brazil. J Oral Pathol Med. 2004;33:7-12.

20) Ghanaei FM, Joukar F, Rabiei M, Dadashzadeh A, Valeshabad AK. Prevalence of Oral Mucosal Lesions in an Adult Iranian Population. Iran Red Crescent Med J. 2013;15: 600-604.

21) Shulman JD, Beach MM, Rivera-Hidalgo F. The prevalence of oral mucosal lesions in U.S. adults: data from the Third National Health and Nutrition Examination Survey, 1988-1994. J Am Dent Assoc. 2004;135:1279-86.

22) Axéll, T. A preliminary report on prevalences of oral mucosal lesions in a Swedish population. Community Dent Oral Epidemiol. 1975;3:143-5.

23) Vieira-Andrade RG, Zuquim Guimarães FF, Vieira CS, Freire ST, Ramos-Jorge ML, Fernandes AM. Oral mucosa alterations in a socioeconomically deprived region: prevalence and associated factors. Bras Oral Res. 2011; 25:393-400.

24) Kleinman DV, Swango PA, Niessen LC. Epidemiologic studies of oral mucosal conditions - methodologic issues. Community Dent Oral Epidemiol. 1991;19:129-40.

25) Dost F, Do L, Farah CS. Lesion Evaluation, Screening and Identification of Oral Neoplasia Study: an assessment of high-risk Australian populations. Community Dent Oral Epidemiol. 2016;44:64-75.

26) Halal IS, Victora CG, Barros FC. Determinantes do hábito de fumar e de seu abandono durante a gestação em localidade urbana na região sul do Brasil. Rev Saude Publica [online]. 1993;27:105-112.

27) Figueiredo SA, Rosalem GC, Cantanhede C, Thomaz AF, da Cruz FN. Systemic alterations and their oral manifestations in pregnant women. J Obstet Gynaecol Res. 2017;43:16-22.

28) Jahanbani J, Morse DE, Alinejad H. Prevalence of oral lesions and normal variants of the oral mucosa in 12 to 15-year-old students in Tehran, Iran. Arch Iran Med 2012;15:142-5.

29) Neville B, Damm DD, Allen C, Chi A. Oral & Maxilofacial Pathology. 4th edn. Amsterdam: Saunders; 2015.

30) Camargo MBJ, Dumith SC, Barros AJD. Uso regular de serviços odontológicos entre adultos: padrões de utilização e tipos de serviços. Cad. Saude Publica. 2009;25:1894-1906.

Table 1. Prevalence of individual variables and oral habits of pregnant women. Pelotas/Brazil (N=2481)*.

Variables	**Prevalence (%)**
Socio-demographic	
Age (groups) (n=2481)	
Adolescent (up to 20 years)	312 (12.58%)
Young adult (21 – 39 years)	2093 (82.36%)
Adult (40 years and over)	76 (3.06%)
Skin color (self-reported) (n=2475)	
White	1769 (71.47%)
Black	331 (13.37%)
Yellow	19 (0.77%)
Brown	346 (13.98%)
Indigenous	7 (0.28%)
IGN**	3 (0.12%)
Schooling (complete years) (n=2480)	
0-4	164 (6.61%)
5-8	537 (21.65%)
9-11	911 (36.73%)
12+	868 (35.00%)
Income (in quintiles) (n=2479)	
1st	400 (16.14%)
2nd	482 (19.44%)
3rd	514 (20.73%)
4th	524 (21.14%)
5th	559 (22.55%)
Oral Habits	
Flossing? (n=1635)	
No, never	930 (37.62%)
Yes sometimes	1040 (42.07%)
Yes, daily	501 (20.27%)
IGN	1 (0.04%)
Bleeding on brushing? (n=2472)	
No	1407 (56.92%)
Yes, sometimes	734 (29.69%)
Yes, almost always	331 (13.39%)
Going to the dentist last month? (n=2472)	
No	910 (36.81%)
Yes	1551 (62.74%)
IGN	11 (0.44%)
Orientations on oral hygiene during pregnancy (n=2472)	
No	2135 (86.37%)
Yes	334 (13.51%)
IGN	3 (0.12%)

*Differences in N are due to losses in some variables.
**IGN: ignored.

Table 2. Groups and characteristics of oral mucosal lesions diagnosed in pregnant women. Pelotas/Brazil (N = 2481)*.

Variable	Prevalence (%)
Groups of Lesions (n=482)	
White and red	9 (1.87%)
Infectious	67 (13.90%)
Swellings	12 (2.49%)
Ulcers	47 (9.75%)
Developmental alterations	262 (54.35%)
Benign oral brownish pigmentation	68 (14.11%)
Other**	17 (3.53%)
Sites** (n=572)	
Lip	39 (6.82)
Vestibule and gums	249 (43.54)
Buccal mucosa/ Labial commissure	38 (6.64)
Hard palate	35 (6.12)
Soft palate and Tonsillar pillar	3 (0.52)
Tongue	199 (34.79)
Floor of the mouth	9 (1.57)
Size of the lesion (n=445)	
≤5mm	125 (28.09)
6-10mm	50 (11.24)
11-20mm	22 (4.94)
>20mm	6 (1.35)
Multiple lesions not measured	242 (54.38)
Duration (referred) (n=447)	
No, had never noticed	168 (37.58)
Less than 1 month	64 (14.32)
Between 1 and 6 months	36 (8.05)
Between 6 and 12 months	12 (2.68)
More than 1 year	167 (37.37)
Associated symptoms (n=220)	
Pain	59 (26.82)
Burning	51 (23.18)
Itching	22 (10.0)
Discomfort	88 (40.0)

*Differences in N are due to losses in some variables.
**Includes lesions classified as "other" in the oral exam, without specific clinical diagnosis.
***The same lesion could involve more than one site, so the total number of sites exceeds the total number of lesions, which is 482.

4 Considerações Finais

Ao analisar os poucos estudos de base populacional sobre prevalência de lesões de mucosa bucal, observou-se que grande parte deles empregou metodologias não padronizadas, o que reduz sua qualidade e confiabilidade e dificulta as comparações entre eles.

Os estudos de coorte conduzidos em Pelotas tem empregado metodologia rigorosa no que diz respeito à amostragem, aos critérios diagnósticos, e ao treinamento e calibração dos entrevistadores e examinadores. Portanto, o estudo com as gestantes, além de ser o primeiro estudo de base populacional que avaliou a ocorrência de LMBs em mulheres no período gestacional, é um exemplo de estudo que pode ser seguido em relação aos seus aspectos metodológicos.

Sendo assim, melhorar a qualidade dos estudos nessa área é fundamental, além de investigar populações ainda pouco conhecidas em relação a desfechos em saúde bucal. O delineamento de condições bucais em populações específicas permite o conhecimento da sua distribuição naquele grupo, podendo favorecer a prevenção de condições patológicas e o esclarecimento desses indivíduos acerca de aspectos relacionados à sua saúde.

Referências

ALI, M.; SUNDARAM, D. Biopsied oral soft tissue lesions in Kuwait: a six-year retrospective analysis. **Medical Principles and Practice**, v.21, n.6, p.569-75, 2012.

AL-MAWERI, S-A; TARAKJI, B.; AL-SUFYANI, G.A.; AL-SHAMIRI, H.M.; GAZAL, G. Lip and oral lesions in children with Down syndrome. A controlled study. **Journal of Clinical and Experimental Dentistry,** v.7, n.2, p.e284-8, 2015.

AXÉLL, T. A preliminary report on prevalences of oral mucosal lesions in a Swedish population. **Community Dentistry and Oral Epidemiology**, v.3, p.143-5, 1975.

AXÉLL, T.; PINDBORG, J.J.; SMITH, C.J.; VAN DER WAAL, I. Oral white lesions with special reference to precancerous and tobacco- related lesions: Conclusions of an international symposium held in Uppsala, Sweden, May 18-21 1994. International Collaborative Group on Oral White Lesions. **Journal of Oral Pathology & Medicine**, v.25, p.49-54, 1996.

BÁNÓCZY, J.; RIGÓ, O. Prevalence study of oral precancerous lesions within a complex screening system in Hungary. **Community Dentistry and Oral Epidemiology**, v.19, p.265-7, 1991.

BARROS, A.J.D.; SANTOS, I.S.; MATIJASEVICH, A.; ARAÚJO, C.L.; GIGANTE, D.P.; MENEZES, A.M.B.; HORTA, B.L.; TOMASI, E.; VICTORA, C.G.; BARROS, F.C. Methods used in the 1982, 1993, and 2004 birth cohort studies from Pelotas, Rio Grande do Sul State, Brazil, and a description of the socioeconomic conditions of participants' families. **Cadernos de Saúde Pública**, v.24, n.3, p.371-80, 2008.

BARROS, M.B.A.; LIMA, M.G.; MEDINA, L.P.B.; SZWARCWALD, C.L.; MALTA, D.C. Social inequalities in health behaviors among Brazilian adults: National Health Survey, 2013. **International Journal for Equity in Health**, v.15, p.148, 2016.

BHATNAGAR, P.; RAI, S.; BHATNAGAR, G.; KAUR. M.; GOEL. S.; PRABHAT, M. Prevalence study of oral mucosal lesions, mucosal variants, and treatment

required for patients reporting to a dental school in North India: In accordance with WHO guidelines. **Journal of Family and Community Medicine**, v.20, n.1, p.41-48, 2013.

BOUQUOT, J.E. Common oral lesions found during a mass screening examination. **The Journal of the American Dental Association,** v.112, p.50-57, 1986.

BYAKODI, R.; SHIPURKAR, A.; BYAKODI, S.; MARATHE, K. Prevalence of Oral Soft Tissue Lesions in Sangli, India. **Journal of Community Health**, v.36, p.756–759, 2011.

CAMARGO, M.B.J; DUMITH, S.C.; BARROS, A.J.D. Uso regular de serviços odontológicos entre adultos: padrões de utilização e tipos de serviços. **Cadernos de Saúde Pública**, v.25, n.9, p.1894-1906, 2009.

CAMPISI, G.; MARGIOTTA, V. Oral mucosal lesions and risk habits among men in an Italian study population. **Journal of Oral Pathology & Medicine**, v.30, p.22-8, 2001.

CARDOSO, J.A.; SPANEMBERG, J.C.; CHERUBINI, K.; FIGUEIREDO, M.A.; SALUM, F.G. Oral granuloma gravidarum: a retrospective study of 41 cases in Southern Brazil. **Journal of Applied Oral Science**, v.21, n.3, p.215-8, 2013.

CARRARD, V.; HAAS, A.; RADOS, P.; FILHO, M.; OPPERMANN, R.; ALBANDAR, J., SUSIN, C. Prevalence and risk indicators of oral mucosal lesions in an urban population from South Brazil. **Oral Diseases**, v.17, 171-9, 2011.

CASTELLANOS, J.L.; DÍAZ-GUZMÁN, L. Lesions of the oral mucosa: an epidemiological study of 23785 Mexican patients. **Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology**, v.105, p.79-85, 2008.

CHUNG, C.H.; YANG, Y.H.; WANG, T.Y.; SHIEH, T.Y.; WARNAKULASURIYA, S. Oral precancerous disorders associated with areca quid chewing, smoking, and alcohol drinking in southern Taiwan. **Journal of Oral Pathology & Medicine,** v.34, p.460-6, 2005.

CORBET, E.F.; HOLMGREN, C.J.; PHILIPSEN, H.P. Oral mucosal lesions in 65-74-year-old Hong Kong Chinese. **Community Dentistry and Oral Epidemiology,** v.22, p.392-5, 1994.

DO, L.G.; SPENCER, A.J.; DOST, F.; FARAH, C.S. Oral mucosal lesions: findings from the Australian National Survey of Adult Oral Health. **Australian Dental Journal,** v.59, p.114-20, 2014.

DOS SANTOS, P.J.; BESSA, C.F.; DE AGUIAR, M.C.; DO CARMO, M.A. Cross-sectional study of oral mucosal conditions among a central Amazonian Indian community, Brazil**. Journal of Oral Pathology & Medicine**, v.33, n.1, p.7-12, 2004.

DOST, F.; DO, L.; FARAH, C.S. Lesion Evaluation, Screening and Identification of Oral Neoplasia Study: an assessment of high-risk Australian populations. **Community Dentistry and Oral Epidemiology**, v.44, p.64-75, 2016.

ESPINOZA, I.; ROJAS, R.; ARANDA, W.; GAMONAL, J. Prevalence of oral mucosal lesions in elderly people in Santiago, Chile. **Journal of Oral Pathology & Medicine**, v.32, p571-5, 2003.

FENG, J.; ZHOU, Z.; SHEN, X.; 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. **Journal of Oral Pathology & Medicine***,* v.44, n.7, p.490-4, 2015.

FIGUERO, E.; CARRILLO-DE-ALBORNOZ, A.; MARTÍN, C.; TOBÍAS, A.; HERRERA, D. Effect of pregnancy on gingival inflammation in systematically healthy women: a systematic review. **Journal of Clinical Periodontaology**, v.40, n.5, p.457-473, 2013.

FIGUEIREDO, C.S.A.; ROSALEM, C.G.C.; CANTANHEDE, A.L.C.; THOMAZ, E.B.A.F.; CRUZ, M.C.F.N. Systemic alterations and their oral manifestations in pregnant women. **Journal of Obstetrics and Gynaecology Research,** v.43, n.1, p.16-22, 2017.

GHANAEI, F.M.; JOUKAR, F.; RABIEI, M.; DADASHZADEH, A.; VALESHABAD, A.K. Prevalence of Oral Mucosal Lesions in an Adult Iranian Population. **Iranian Red Crescent Medical Journal,** v.15, p.600-604, 2013.

GHENO, J.N.; MARTINS, M.A.T.; MUNERATO, M.C.; HUGO, F.N.; SANTANA FILHO, M.; WEISSHEIMER, C.; CARRARD, V.C.; MARTINS, M.D. Oral mucosal lesions and their association with sociodemographic, behavioral, and health status factors. **Brazilian Oral Research**, v.29, n.1, p.1-6, 2015.

HAAS, A.N.; GAIO, E.J.; WAGNER, M.C.; RIOS, F.S.; COSTA, R.S.A.; RÖSING, C.K.; OPPERMANN, R.V.; ALBANDAR, J.; SUSIN, C. Um estudo de

coorte de base populacional de saúde bucal no sul do Brasil: Estudo de Porto Alegre. **Revista Brasileira de Epidemiologia,** v.18, n.2, p.515-519, 2015.

HALLAL, P.C.; BERTOLDI, A.D.; DOMINGUES, M.R.; SILVEIRA, M.F.D.; DEMARCO, F.F.; DA SILVA, I.C.M.; BARROS, F.C.; VICTORA, C.G.; BASSANI, D.G. Cohort Profile: The 2015 Pelotas (Brazil) Birth Cohort Study. **International Journal of Epidemiology,** 2017. [Epub ahead of print].

HALAL, I.S.; VICTORA, C.G.; BARROS, F.C. Determinantes do hábito de fumar e de seu abandono durante a gestação em localidade urbana na região sul do Brasil. **Revista de Saúde Pública** [online], v.27, n.2, p.105-112, 1993.

HOLDE, G.E.; OSCARSON, N.; TILLBERG, A.; MARSTRANDER, P. JÖNSSON, B. Methods and background characteristics of the TOHNN study: a population-based study of oral health conditions in northern Norway. **International Journal of Circumpolar Health**, v.76, n.30169, 2016.

IBGE - INSTITUTO BRASILEIRO DE GEOGRAFIA E ESTATÍSTICA. Disponível em: < https://www.ibge.gov.br/index.php>. Acesso em 07 mai. 2018.

KASSEBAUM, N.J.; BERNABÉ, E.; DAHIYA, M.; BHANDARI, B.; MURRAY, C.J..; MARCENES, W. Global burden of severe periodontitis in 1990-2010: a systematic review and meta-regression. **Journal of Dental Research**, v.93, p.1045-53, 2014.

KLEINMAN, D.V., SWANGO, P.A., NIESSEN, L.C. Epidemiologic studies of oral mucosal conditions - methodologic issues. **Community Dentistry and Oral Epidemiology**, v.19, p.129-40, 1991.

KLEINMAN, D.V.; SWANGO, P.A.; PINDBORG, J.J. Epidemiology of oral mucosal lesions in United States schoolchildren: 1986-87. **Community Dentistry and Oral Epidemiology**, v.22, p.243-53, 1994.

KOAY, C.L.; LIM, J.A.; SIAR, C.H. The prevalence of tongue lesions in Malaysian dental outpatients from the Klang Valley area. **Oral Diseases**; v.17, n.2, p.210-6, 2011.

KRAMER, I.R.; PINDBORG, J.J.; BEZROUKOV, V.; INFIRRI, J.S. Guide to epidemiology and diagnosis of oral mucosal diseases and conditions. World Health Organization. **Community Dentistry and Oral Epidemiology**, v.8, n.1, p.1-26, 1980.

KRISHNAPILLAI, R.; PUNNOOSE, K.; ANGADI, P.V.; KONERU, A. Oral pyogenic granuloma--a review of 215 cases in a South Indian Teaching

Hospital, Karnataka, over a period of 20 years. **Oral and Maxillofacial Surgery**, v.16, n.3, p.305-9, 2012.

JAHANBANI, J.; MORSE, D.E.; ALINEJAD, H. Prevalence of oral lesions and normal variants of the oral mucosa in 12 to 15-year-old students in Tehran, Iran. **Archives of Iranian Medicine**, v.15, n.3, p.142-5, 2012.

LIMA, G.S.; FONTES, S.T.; DE ARAÚJO, L.M.; ETGES, A.; TARQUINIO, S.B.; GOMES, A.P. A survey of oral and maxillofacial biopsies in children: a single-center retrospective study of 20 years in Pelotas-Brazil. **Journal of Applied Oral Science**, v.16, n.6, p.397-402, 2008.

LIN, H.C.; CORBET, E.F.; LO, E.C. Oral mucosal lesions in adult Chinese. **Journal of Dental Research**, v**.**80, p.1486-90, 2001.

LONEY, P.L.; CHAMBERS, L.W.; BENNETT, K.J.; ROBERTS, J.G.; STRATFORD, P.W. Critical appraisal of the health research literature: prevalence or incidence of a health problem. **Chronic Diseases in Canada**, v.19, p.170-176, 1998.

MACENTEE, M.I.; GLICK, N.; STOLAR, E. Age, gender, dentures and oral mucosal disorders. **Oral Diseases**, v.4, p.32-6, 1998.

MAJORANA, A.; BARDELLINI, E.; FLOCCHINI, P.; AMADORI, F.; CONTI. G.; CAMPUS, G. Oral mucosal lesions in children from 0 to 12 years old: tem years' experience. **Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology,** v**.**110, p.13-18, 2010.

MENDEZ, M.; CARRARD, V.C.; HAAS, A.N.; LAUXEN, I.S.; BARBACHAN, J.J.; RADOS, P.V.; SANT'ANA FILHO, M. A 10-year study of specimens submitted to oral pathology laboratory analysis: lesion occurrence and demographic features. **Brazilian Oral Research**, v.26, p.235-41, 2012.

MIDDLETON, P.; ESPOSITO, M.; IHEOZOR-EJIOFOR, Z. Treating periodontal disease for preventing adverse birth outcomes in pregnant women. **Cochrane Database of Systematic Reviews,** v.12, 2015.

MOHER, D.; LIBERATI, A.; TETZLAFF, J.; ALTMAN, D.G.; PRISMA GROUP. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. **Journal of Clinical Epidemiology,** v.62, p.1006-12, 2009.

MUMCU G.; CIMILLI, H.; SUR, H.; HAYRAN, O.; ATALAY, T. Prevalence and distribution of oral lesions: a cross-sectional study in Turkey. **Oral Diseases**. v.11, p.81-7, 2005.

NEVILLE, Brad; DAMM, Douglas; ALLEN, Carl; CHI, Angela. **Oral & Maxilofacial Pathology**. 4th edn. Amsterdam: Saunders; 2015. 928p.

OLIVEIRA, L.J.; TORRIANI, D.D.; CORREA, M.B.; PERES, M.A.; PERES, K.G.; MATIJASEVICH, A.; DOS SANTOS, I.S.; BARROS, A.J.; DEMARCO, F.F.; TARQUINIO, S.B. Oral mucosal lesions' impact on oral health-related quality of life in preschool children. **Community Dentistry and Oral Epidemiology**, v.43, n.6, p.578-85, 2015.

OSTERBERG, T.; OHMAN, A.L.; HEYDEN, G.; SVANBORG, A. The condition of the oral mucosa at age 70: a population study. **Gerodontology***,* v.4, p.71-5, 1985.

PARLAK, A.H.; KOYBASI, S.; YAVUZ, T.; YESILDAL, N.; ANUL, H.; AYDOGAN, I.; CETINKAYA, R.; KAVAK, A. Prevalence of oral lesions in 13- to 16-year-old students in Duzce, Turkey. **Oral Diseases**, v.12, p.553-8, 2006.

PELOTAS (BRAZIL) BIRTH COHORTS. Disponível em: <http://www.epidemio-ufpel.org.br/site/content/estudos/index.php>. Acesso em 07 mai. 2018.

PESSÔA, C.P.; ALVES, T.D.; DOS SANTOS, N.C.; DOS SANTOS, H.L.; AZEVEDO, A.D.E.; DOS SANTOS, J.N.; OLIVEIRA, M.C. Epidemiological survey of oral lesions in children and adolescents in a Brazilian population. **International Journal of Pediatric Otorhinolaryngology,** v.79, n.11, p.1865-71, 2015.

RAMOS-E-SILVA, M.; MARTINS, N.R. Oral and Genital Changes in Pregnancy. **Clinics in Dermatology**; v.34, n.3, p.353-358, 2016.

REDDY, S.S.; PRASHANTH, R.; YASHODHA, D.B.K.; CHUGH, N.; KAUR. A.; THOMAS, N. Prevalence of oral mucosal lesions among chewing tobacco users: A cross-sectional study. **Indian Journal of Dental Research**, v.26, n.5, p.537-541, 2015.

REICHART, P.A. Oral mucosal lesions in a representative cross-sectional study of aging Germans. **Community Dentistry and Oral Epidemiology,** v.28, p.390-8, 2000.

ROED-PETERSEN, B.; RENSTRUP, G. A topographical classification of the oral mucosa suitable for electronic data processing. Its application to 560 leukoplakias. **Acta Odontologica Scandinavica**, v.27, p.681-95, 1969.

SALONEN, L.; AXÉLL, T.; HELLDÉN, L.J. Occurrence of oral mucosal lesions, the influence of tobacco habits and an estimate of treatment time in an adult Swedish population. **Journal of Oral Pathology & Medicine**, v.19, p.170-6, 1990.

SAWYER, D.R.; TAIWO, E.O.; MOSADOMI, A. Oral anomalies in Nigerian children. **Community Dentistry and Oral Epidemiology**, v.12, p.269-73, 1984.

SAWYER, S.M.; AZZOPARDI, P.S.; WICKREMARATHNE, D.; PATTON, G.C. The age of adolescence. **The Lancet Child & Adolescent Health**, v.2, p.223-228, 2018.

SEDANO, H.O.; CARREON FREYRE, I.; GARZA DE LA GARZA, M.L.; GOMAR FRANCO, C.M.; GRIMALDO HERNANDEZ, C.; HERNANDEZ MONTOYA, M.E.; HIPP, C.; KEENAN, K.M.; MARTINEZ BRAVO, J.; MEDINA LÓPEZ, J.A. Clinical orodental abnormalities in Mexican children. **Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology,** v. 68, p.300-11, 1989.

SEDANO, H.O. Congenital oral anomalies in Argentinian children. **Community Dentistry and Oral Epidemiology,** v.3, p.61-3, 1975.

SERVATO, J.P.; DE PAULO, L.F.; DE FARIA, P.R.; CARDOSO, S.V.; LOYOLA, A.M. Metastatic tumours to the head and neck: retrospective analysis from a Brazilian tertiary referral centre. **International Journal of Oral and Maxillofacial Surgery**, v.42, n.11, p.1391-6, 2013.

SHULMAN, J.D.; BEACH, M.M.; RIVERA-HIDALGO, F. The prevalence of oral mucosal lesions in U.S. adults: data from the Third National Health and Nutrition Examination Survey, 1988-1994. **The Journal of the American Dental Association**, v.135, p.1279-86, 2004.

SHULMAN, J.D. Prevalence of oral mucosal lesions in children and youths in the USA. **International Journal of Paediatric Dentistry**, v.15, p.89-97, 2005.

SMEDBERG, J.; LUPATTELLI, A.; MÅRDBY, A.C.; ØVERLAND, S.; NORDENG, H. The relationship between maternal depression and smoking cessation during pregnancy - a cross-sectional study of pregnant women from 15 European countries. **Archives of Women's Mental Health,** v.18, n.1, p.73-84, 2015.

SPLIETH, C.H.; SÜMNIG, W.; BESSEL, F.; JOHN, U.; KOCHER, T. Prevalence of oral mucosal lesions in a representative population. **Quintessence International,** v. 38, p.23-9, 2007.

SULIMAN, N.M.; JOHANNESSEN, A.C.; ALI, R.W.; SALMAN, H.; ÅSTRØM, A.N. Influence of oral mucosal lesions and oral symptoms on oral health related quality of life in dermatological patients: a cross sectional study in Sudan. **BMC Oral Health**, v.12, n.19, p.11, 2012.

SYKARA, M.; NTOVAS, P.; KALOGIROU, E.M.; TOSIOS, K.I.; SKLAVOUNOU, A. Oral lymphoepithelial cyst: A clinicopathological study of 26 cases and review of the literature. **Journal of Clinical and Experimental Dentistry,** v.9, p.1035-1043, 2017.

TARQUINIO, S.B.; DE OLIVEIRA, L.J.C.; CORREA, M.B.; PERES, M.A.; PERES, K.G.; GIGANTE, D.P.; HORTA, B.L.; DEMARCO, F.F. Factors associated with prevalence of oral lesions and oral self-examination in young adults from a birth cohort in Southern Brazil. **Cadernos de Saúde Pública**, v.29, n.1, p.155-164, 2013.

THOMAZ, E.B.A.F.; ALVES, C.M.C.; RIBEIRO, C.C.C.; BATISTA, R.F.L., SIMÕES, V.M.F.; CAVALLI, R.; SARAIVA, M.C.; CARDOSO, V.C.; BETTIOL, H.; BARBIERI, M.A.; SILVA, A.A.M. Desfechos perinatais e alterações na cavidade bucal: coortes brasileiras de Ribeirão Preto e São Luís. **Revista Brasileira de Epidemiologia [online],** v.18, n.4, p.966-970, 2015.

VIEIRA-ANDRADE, R.G.; MARTINS-JÚNIOR, P.A.; CORRÊA-FARIA, P.; STELLA, P.E.; MARINHO, S.A.; MARQUES, L.S.; RAMOS-JORGE, M.L. Oral mucosal conditions in preschool children of low socioeconomic status: prevalence and determinant factors. **European Journal of Pediatrics,** v.172, p.675-81, 2013.

UCHOA-VASCONCELOS, A.C.; FILIZOLA-DE OLIVEIRA, D.J.; ROMAN-MARTELLI, S.J.; ETGES, A.; NEUTZLING-GOMES, A.P.; CHAVES-TARQUINIO, S.B. Demographic profile of oral nonodontogenic cysts in a Brazilian population. **Medicina Oral Patologia Oral y Cirugia Bucal,** v.19, p.308-312, 2014.

VILLANUEVA-VILCHIS, M.C.; LÓPEZ-RÍOS, P.; GARCÍA, I.M.; GAITÁN-CEPEDA, L.A. Impact of oral mucosa lesions on the quality of life related to oral health. An etiopathogenic study. **Medicina Oral Patologia Oral y Cirugia Bucal**, v.21, n.2, p.e178-84, 2016.

WITKOP, C.J.; BARROS, L. Oral and Genetic Studies of Chileans 1960. Oral anomalies. **American Journal of Physical Anthropology***,* v.21, p.15-24, 1963.

World Health Organization (WHO). **Oral health surveys**: basic methods. 4th edn. WHO: Geneva; 1980. 125p.

ZAIN, R.B.; IKEDA, N.; RAZAK, I.A.; AXÉLL, T.; MAJID, Z.A.; GUPTA, P.C.; YAACOB, M. A national epidemiological survey of oral mucosal lesions in Malaysia. **Community Dentistry and Oral Epidemiology**, v.25, p.377-83, 1997.

Apêndices

Apêndice A – Estratégia de busca no Pubmed

SUPLEMENTAR MATERIAL I (Community Dentistry and Oral Epidemiology)

Table 1 – Search strategy used in PubMed (MEDLINE)

	Search terms
#3	Search #1 AND #2
#2	“Oral mucosal diseases” OR “Oral lesions” OR “Buccal lesions” OR “Lichen Planus, Oral” OR “Oral Lichen Planus” OR “Leukoedema, Oral” OR “Leukoedemas, Oral” OR “Oral Leukoedema” OR “Oral Leukoedemas” OR “Lip Diseases” OR “Disease, Lip” OR “Diseases, Lip” OR “Lip Disease” OR “Cheilitis” OR “Cheilitides” OR “Cleft Lip” OR “Cleft Lips” OR “Lip, Cleft” OR “Lips, Cleft” OR “Harelip” OR “Harelips” OR “Cleft palate” OR “Cleft Palates” OR “Palate, Cleft” OR “Palates, Cleft” OR “Cleft Palate, Isolated” OR “Herpes Labialis” OR “Herpes Simplex, Labial” OR “Labial Herpes Simplex” OR “Lip Neoplasms” OR “Lip Neoplasm” OR “Neoplasm, Lip” OR “Neoplasms, Lip” OR “Cancer of Lip” OR “Lip Cancers” OR “Cancer of the Lip” OR “Lip Cancer” OR “Cancer, Lip” OR “Cancers, Lip” OR “Candidiasis, Oral” OR “Candidiases, Oral” OR “Oral Candidiases” OR “Oral Candidiasis” OR “Moniliasis, Oral” OR “Moniliases, Oral” OR “Oral Moniliases” OR “Oral Moniliasis” OR “Mouth Neoplasms” OR “Mouth Neoplasm” OR “Neoplasm, Mouth” OR “Neoplasms, Oral” OR “Neoplasm, Oral” OR “Oral Neoplasm” OR “Oral Neoplasms” OR “Neoplasms, Mouth” OR “Cancer of Mouth” OR “Mouth Cancers” OR “Mouth Cancer” OR “Cancer, Mouth” OR “Cancers, Mouth” OR “Oral Cancer” OR “Cancer, Oral” OR “Cancers, Oral” OR “Oral Cancers” OR “Cancer of the Mouth” OR “Gingival Neoplasms” OR “Neoplasms, Gingival” OR “Gingival Neoplasm” OR “Neoplasm, Gingival” OR “Leukoplakia, Oral” OR “Leukoplakias, Oral” OR “Oral Leukoplakia” OR “Oral Leukoplakias” OR “Leukokeratosis, Oral” OR “Leukokeratoses, Oral” OR “Oral Leukokeratoses” OR “Oral Leukokeratosis” OR “Keratosis, Oral” OR “Palatal Neoplasms” OR “Neoplasm, Palatal” OR “Neoplasms, Palatal” OR “Palatal Neoplasm” OR “Mucositis” OR “Mucositides” OR “Oral Fistula” OR “Fistula, Oral” OR “Fistulas, Oral” OR “Oral Fistulas” OR “Dental Fistula” OR “Gingival Fistula” OR “Fistula, Gingival” OR “Fistulas, Gingival” OR “Gingival Fistulas” OR “Fistulas, Dental” OR “Dental Fistulas” OR “Fistula, Dental” OR “parulis” OR “Ranula” OR “Ranulas” OR “Oral Ulcer” OR “Oral Ulcers” OR “Ulcer, Oral” OR “Ulcers, Oral” OR “Mouth Ulcer” OR “Mouth Ulcers” OR “Ulcer, Mouth” OR “Ulcers, Mouth” OR “Stomatitis, Aphthous” OR “Aphthous Stomatitides” OR “Aphthous Stomatitis” OR “Stomatitides, Aphthous” OR “Ulcer, Aphthous” OR “Aphthous Ulcer” OR “Aphthous Ulcers” OR “Ulcers, Aphthous” OR “Aphthae” OR “carcinoma, squamous cell” OR “Stomatitis” OR “Stomatitides” OR “Oral Mucositis” OR “Mucositides, Oral” OR “Oral Mucositides” OR “Oromucositis” OR “Oromucositides” OR “Mucositis, Oral” OR “Stomatitis, Denture” OR “Denture Stomatitides” OR “Denture Stomatitis” OR “Stomatitides, Denture” OR “Stomatitis, Herpetic” OR “Herpetic Stomatitides” OR “Herpetic Stomatitis” OR “Stomatitides, Herpetic” OR “Herpes Simplex, Oral” OR “Oral Herpes Simplex” OR “Simplex, Oral Herpes” OR “Gingivostomatitis, Herpetic” OR “Gingivostomatitides, Herpetic” OR “Herpetic Gingivostomatitides” OR “Herpetic Gingivostomatitis” OR “Head and Neck Neoplasms” OR “Carcinoma, Squamous Cell” OR “Carcinomas, Squamous Cell” OR “Squamous Cell Carcinomas” OR “Squamous Cell Carcinoma” OR

	“Carcinoma, Squamous” OR “Carcinomas, Squamous” OR “Squamous Carcinoma” OR “Squamous Carcinomas” OR “Carcinoma, Epidermoid” OR “Carcinomas, Epidermoid” OR “Epidermoid Carcinoma” OR “Epidermoid Carcinomas” OR “Carcinoma, squamous cell of head and neck” OR “Squamous Cell Carcinoma, Head And Neck” OR “Squamous cell carcinoma of the head and neck” OR “Carcinoma, squamous cell oral” OR “Gingivitis, Necrotizing Ulcerative” OR “Necrotizing Ulcerative Gingivitis” OR “Ulcerative Gingivitis, Necrotizing” OR “Oral Submucous Fibrosis” OR “Fibroses, Oral Submucous” OR “Fibrosis, Oral Submucous” OR “Oral Submucous Fibroses” OR “Submucous Fibroses, Oral” OR “Submucous Fibrosis, Oral” OR “Noma” OR “Nomas” OR “Stomatitis, Gangrenous” OR “Gangrenous Stomatitides” OR “Gangrenous Stomatitis” OR “Stomatitides, Gangrenous” OR “Cancrum Oris” “chancre” OR “syphilis” OR “Acute necrotizing gingivitis” OR “Acute herpetic gingivostomatitis” OR “coated tongue” OR “Geographic tongue” OR “Oral pigmentation” OR “Exostoses oral” OR “mandibular torus” OR “palatine torus” OR “Varicosities oral” OR “varicose veins oral” OR “Leukokeratosis nicotina palati” OR “Leukokeratosis nicotine palati” OR “Tongue, Fissured” OR “mucocele” OR “Erythroplakia oral” OR “granuloma, pyogenic” OR “Fordyce granules” OR “Fibroma Oral”
#1	“Longitudinal Studies” OR “Longitudinal Survey” OR “Longitudinal Surveys” OR “prospective study” OR “prospective studies” OR “cohort” OR “cohort study” OR “cohort studies” OR “cohort analysis” OR “cross-sectional studies” OR “cross-sectional study” OR “cross-sectional analysis” OR “cross-sectional analyses” OR “cross-sectional survey” OR “cross sectional survey” OR “cross-sectional surveys” OR “observational study” OR “observational studies” OR “epidemiologic study” OR “epidemiologic studies” OR “epidemiological study” OR “epidemiological studies” OR “prevalence study” OR “prevalence studies” OR “population-based study” OR “population-based studies” OR “Censuses” OR “Census” OR “Census Methods” OR “Census Method” OR “Method, Census” OR “Methods, Census” OR “Microcensus”

Apêndice B – Artigos excluídos da revisão sistemática após leitura completa.

SUPPLEMENTAR MATERIAL II (Community Dentistry and Oral Epidemiology)

Excluded articles (after full text analysis).

Not population-based studies:

1) Ikeda N, Handa Y, Khim SP, et al. Prevalence study of oral mucosal lesions in a selected Cambodian population. *Community Dent Oral Epidemiol.* 1995;23(1):49-54.
2) Lay KM, Sein K, Myint A, Ko SK, Pindborg JJ. Epidemiologic study of 600 villagers of oral precancerous lesions in Bilugyun: preliminary report. *Community Dent Oral Epidemiol.* 1982;10(3):152-5.
3) Lynge Pedersen AM, Nauntofte B, Smidt D, Torpet LA. Oral mucosal lesions in older people: relation to salivary secretion, systemic diseases and medications. *Oral Dis.* 2015;21(6):721-9.
4) Taiwo JO, Kolude B, Akinmoladun V. Oral mucosal lesions and temporomandibular joint impairment of elderly people in the South East Local Government Area of Ibadan. *Gerodontology.* 2009;26(3):219-24.
5) Bouquot JE. Common oral lesions found during a mass screening examination. *J Am Dent Assoc.* 1986;112(1):50-7.
6) Robledo-Sierra J, Mattsson U, Svedensten T, Jontell M. The morbidity of oral mucosal lesions in an adult Swedish population. *Med Oral Patol Oral Cir Bucal.* 2013;18(5):e766-72.
7) Angulo-Núñez JJ, Rodríguez-Archilla *A.* Lesiones de la mucosa bucal en pacientes de Mérida, Venezuela. *Invest Clin.* 2015;56(4):367-376.
8) Farah CS, Simanovic B, Savage NW. Scope of practice, referral patterns and lesion occurrence of an oral medicine service in Australia. *Oral Dis.* 2008;14(4):367-75.
9) Pearson N, Croucher R, Marcenes W, O'Farrell M. Prevalence of oral lesions among a sample of Bangladeshi medical users aged 40 years and over living in Tower Hamlets, UK. *Int Dent J.* 2001;51(1):30-4.
10) Vigilid M. Oral mucosal lesions among institutionalized elderly in Denmark. *Community Dent Oral Epidemiol.* 1987;15(6):309-13.
11) Crivelli MR, Aguas S, Adler I, Quarracino C, Bazerque P. Influence of socioeconomic status on oral mucosa lesion prevalence in schoolchildren. *Community Dent Oral Epidemiol.* 1988;16(1):58-60.
12) Glazar I, Urek MM, Brumini G, Pezelj-Ribaric S. Oral sensorial complaints, salivary flow rate and mucosal lesions in the institutionalized elderly. *J Oral Rehabil.* 2010;37(2):93-9.
13) Mozafari PM, Dalirsani Z, Delavarian Z, et al. Prevalence of oral mucosal lesions in institutionalized elderly people in Mashhad, Northeast Iran. *Gerodontology.* 2012;29(2):e930-4.

14) Pentenero M, Broccoletti R, Carbone M, Conrotto D, Gandolfo S. The prevalence of oral mucosal lesions in adults from the Turin area. *Oral Dis.* 2008;14(4):356-66.

Studies in which oral mucosal lesions prevalence was not the objective:

1) Vieira-Andrade RG, Martins-Júnior PA, Corrêa-Faria P, Marques LS, Paiva SM, Ramos-Jorge ML. Impact of oral mucosal conditions on oral health-related quality of life in preschool children: a hierarchical approach. *Int J Paediatr Dent.* 2015;25(2):117-26.
2) Abreu LP, Kruger E, Tennant M. Oral cancer in Western Australia, 1982-2006: a retrospective epidemiological study. *J Oral Pathol Med.* 2010;39(5):376-81.

Studies with same samples used in another main study already included:

1) Taiyeb Ali TB, Razak IA, Raja Latifah RJ, Zain RB. An epidemiological survey of oral mucosal lesions among elderly Malaysians. *Gerodontology.* 1995;12(1):37-40.

Study was available only as a thesis:

1) Axéll T. A preliminary report on prevalences of oral mucosal lesions in a Swedish population. *Community Dent Oral Epidemiol.* 1975;3(3):143-5.

Apêndice C – Referências usadas na condução dos estudos incluídos na revisão sistemática

SUPPLEMENTAR MATERIAL III (Community Dentistry and Oral Epidemiology)

References adopted to conduct the study, in terms of examiners training and data collection.

Axéll T. A prevalence study of oral mucosa lesions in an adult Swedish population. *Odontol Revy Suppl*. 1976;36:1-103.

Axéll T. Occurrence of leukoplakia and some other oral white lesions among 20333 adult Swedish people. *Community Dent Orat Epidemiol*. 1987;15:46-51.

Axéll T, Holmstrup P, Kramer IRH, Pindborg JJ, Shear M. International seminar on oral leukoplakia and associated lesions related to tobacco habits. *Community Dent Oral Epidemiol*. 1984;12:145-54.

Axéll T, Mornstad H, Sundström B. The relation of the clinical picture to the histopathology of snuff dipper's lesions in a Swedish population. *J Oral Pathol.* 1976;5:229-36.

Axéll T, Pindborg JJ, Smith CJ, van der Wall I. International Collaborative Group on Oral White Lesions. Oral white lesions with special reference to precancerous tobacco-related lesions: conclusions of an international symposium held in Uppsala, Sweden, May 18-21, 1994. *J Oral Pathol Med*. 1996;25:49–54.

Bessa CF, Santos PJ, Aguiar MC, do Carmo MA. Prevalence of oral mucosal alterations in children from 0 to 12 years old. *J Oral Pathol Med*. 2004;33:17-22.

Do LG, Spencer AJ, Dost F, Farah CS. Oral mucosal lesions: findings from the Australian National Survey of Adult Oral Health. Aust Dent J. 2014;59:114-20.

Greer RO, Poulsen TC. Oral tissue alterations associated with the use of smokeless tobacco by teen-agers. *Oral Surg Oral Med Oral Pathol*. 1983;56:275-84.

Hipólito RA, Martins CR. Prevalence of oral mucosal alterations in Brazilian adolescents held in two juvenile re-education centers. *Cien Saude Colet*. 2010;15:3233-43.

Ikeda N, Zain RB, Handa Y, Axéll T. Criteria for diagnosis of oral mucosal lesions. An aid for examiners of epidemiological surveys in South East Asia. In: Zain RB, Ikeda N, Yaacob MBH, eds. Oral mucosal lesions survey of adults in Malaysia. 1995.

Kramer JR, Pindborg JJ, Bezronakov V, Infirri JS. Guide to epidemiology and diagnosis of oral mucosal diseases and conditions. *Community Dent Oral Epidemiol.* 1980;8(1):1-26.

Melnick SL, Nowjack-Raymer R, Kleinman DV, Swango PA. A guide for epidemiological studies of oral manifestations of HIV infection. Geneva: WHO; 1993. 27p.

National Center for Health Statistics. National Health and Nutrition Examination Survey III (NHANES III) - oral examination component. Hyattsville, Md.: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics; 1992.

Neville BW, Damn DD, Allen CM, Bouquot JE. Patologia oral e maxilofacial. Rio de Janeiro: Guanabara Koogan; 2009. 960p.

Pindborg JJ. Atlas of diseases of the oral mucosa. Copenhagen: Munksgaard; 1985. 357p.

Ramanathan J, Leclercq M-H, Mendis BRRN, Barmes DE. Gathering Data on Oral Mucosal Diseases – A New Approach. *World Health Forum*. 1995;16:299-304.

Reichart P, Mohr U, Srisuwan S, Geerlings H, Theetranont C, Kangwanpong T. Precancerous and other oral mucosallesions related to chewing, smoking and drinking habits in Thailand. *Community Dent Oral Epidemiol*. 1987;15:152-60.

Reichart P, Schulz P, Walz C, Beyer D, Pape HD, Hausamen JE et al. Früherkennung von Neubildungen im Kiefer - Gesichtsbereich durch den praktizierenden Zahnarzt. Bonn: Deutsche Krebshilfe/Bundesverband der Deutschen Zahnärzte eV, 1993:16–22.

Roed-Petersen B, Renstrup G. A topographical classification of the oral mucosa suitable for electronic data processing. Its application to 560 leukoplakias. *Acta Odontol Scand.* 1969;27:681-95.

Scully C. Clinical diagnostic methods for the detection of premalignant and early malignant oral lesions. *Community Dent Health*. 1993;10:43-52.

Scully C, Cawson R. Handbook of oral diseases. 2nd edn. London: Martin Dunitz; 1999. 176p.

Slade G, Roberts-Thomson K, Ellershaw A. Survey aims and methods. In: Slade GD, Spencer AJ, Roberts-Thomson KF, eds. Australia's dental generations: the National Survey of Adult Oral Health 2004–06. 2007. p.11-27.

World Health Organization (WHO). Application of the international classification of diseases to dentistry and stomatology. 2nd edn. Geneva: WHO; 1978. 151p.

World Health Organization (WHO). Application of the international classification of diseases to dentistry and stomatology (ICD-DA). 3rd edn. Geneva: WHO; 1995. 248p.

World Health Organization (WHO). Definition of leukoplakia and related lesions: An aid to studies on oral precancer. *Oral Surg Oral Med Oral Pathol*. 1978;46:518-39.

World Health Organization (WHO). Oral health surveys: basic methods. 2nd edn. Geneva: WHO; 1977. 68p.

World Health Organization (WHO). Oral health surveys: basic methods. 3rd edn. Geneva: WHO; 1987. 53p.

World Health Organization (WHO). Oral health surveys: basic methods. 4th edn. Geneva: WHO; 1997. 66p.

Zain RB, Ikeda N, Yaacob M. Oral mucosal lesions survey of adults in Malaysia. Malaysia: Ministry of Health; 1995.

Zain RB, Razak IA, Ikeda N, Axéll T, Downer MC. Training examiners for a national epidemiological survey of oral mucosal lesions. *Int Dent J*. 1996;46:536-42.

Apêndice D

UNIVERSIDADE FEDERAL DE PELOTAS
PROGRAMAS DE PÓS-GRADUAÇÃO EM
EPIDEMIOLOGIA E ODONTOLOGIA

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO - TCLE

A Sra está sendo convidada a participar da pesquisa **"As condições de saúde bucal das mães durante a gravidez podem afetar negativamente os resultados da gravidez e a saúde bucal dos filhos? Um estudo em uma coorte de base populacional no Sul do Brasil".** Sua colaboração neste estudo é MUITO IMPORTANTE, mas a decisão de participar é VOLUNTÁRIA, o que significa que a Sra. terá o direito de decidir se quer ou não participar, bem como de desistir de fazê-lo a qualquer momento.
Esta pesquisa tem como objetivo conhecer a situação de saúde geral e de saúde bucal das gestantes que terão seus filhos acompanhados neste estudo de coorte e sua relação com condições socioeconômicas, demográficas, de acesso a serviços e comportamentos para a saúde.

Garantimos que será mantida a CONFIDENCIALIDADE das informações e o ANONIMATO. Ou seja, o seu nome não será mencionado em qualquer hipótese ou circunstância, mesmo em publicações científicas. NÃO HÁ RISCOS quanto à sua participação na pesquisa, e o exame bucal é simples e rápido. Os BENEFÍCIOS serão, além conhecer a realidade da saúde dos futuros moradores de Pelotas, a qual poderá melhorar os serviços de saúde em sua comunidade, nos casos em que alguma alteração da mucosa bucal for encontrada, a Sra será encaminhada para avalição e tratamento no Centro de Diagnóstico de Doenças da Boca da UFPel.

Será realizada uma entrevista e verificaremos algumas condições de saúde da sua boca, como por exemplo, a presença de cárie e a existência de sangramento nas gengivas. Este exame será realizado por dentistas e não oferece nenhum risco, não causa dor alguma e todos os instrumentos utilizados estarão esterilizados ou serão descartáveis. Em caso de dúvida a senhora poderá entrar em contato com Professor Flávio Fernando Demarco, coordenador desta pesquisa, nos Programas de Pós-Graduação em Odontologia e Epidemiologia da UFPel, pelo telefone (53) 3222 4162 – ramal 130 ou e-mail: ffdemarco@gmail.com.

Eu,.....,
declaro estar esclarecida sobre os termos apresentados e consinto por minha livre e espontânea vontade em participar desta pesquisa e assino o presente documento em duas vias de igual teor e forma, ficando uma em minha posse.

Pelotas, _____ de _____ de 201_.

_____

(Assinatura do participante)

Apêndice E – Ficha de coleta do exame bucal

Ficha de Exame Clínico - Saúde Bucal

Coorte 2015

Nome: _____ *Examinador:* _____

Número: _____ *Anotador:* _____

← *Voltar / Seguir* →

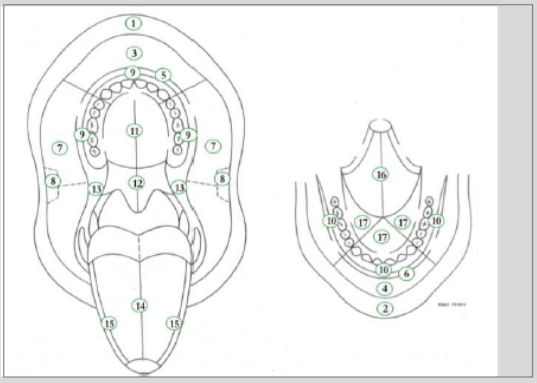
Data do Exame: _____

Lesões Bucais

1. Tu costumas examinar a tua boca? **Códigos** _____ (0) Nunca

2. Presença de lesão bucal? **Códigos** _____ *(0) Não*

3. Localização da **lesão 1** **Códigos**



_____ #N/D

_____ #N/D

_____ #N/D

_____ #N/D

_____ #N/D

_____ #N/D

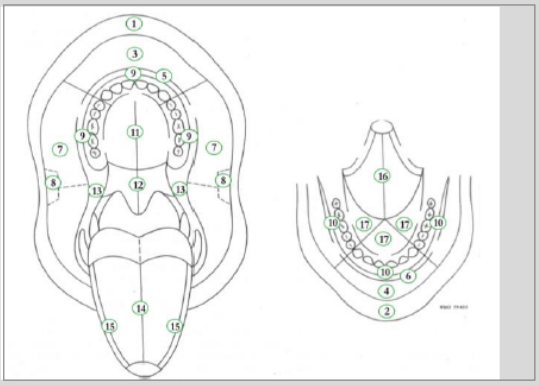
4. Diagnóstico **lesão1** Códigos ##

5. Qual o tamanho da **lesão 1** Códigos mm

** (Usar uma escala em milímetros) **(77)** "Múltiplas lesões não medidas" (88) NSA*

6. Tu já tinhas percebido esta ferida **(Lesão 1)** ou machucado na tua boca? Há quanto tempo?
Códigos ##

7. Localização da **lesão 2** Códigos



#N/D
#N/D
#N/D
#N/D
#N/D
#N/D

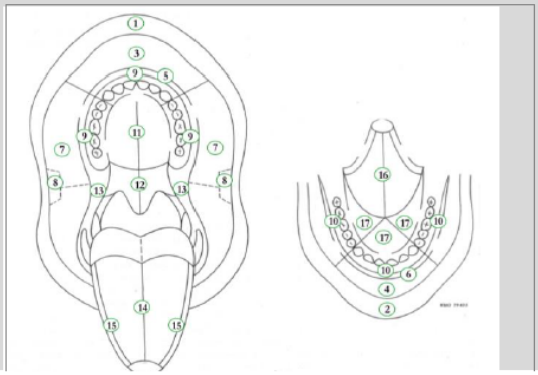
8. Diagnóstico **lesão2** Códigos ##

9. Qual o tamanho da **lesão 2** Códigos mm

** (Usar uma escala em milímetros) **(77)** "Múltiplas lesões não medidas" (88) NSA*

10. Tu já tinhas percebido esta ferida **(Lesão 2)** ou machucado na tua boca? Há quanto tempo?
Códigos ##

11. Localização da **lesão 3** Códigos



#N/D
#N/D
#N/D
#N/D
#N/D
#N/D

12. Diagnóstico **lesão3** Códigos ##

13. Qual o tamanho da **lesão 3** Códigos mm

** (Usar uma escala em milímetros) **(77)** "Múltiplas lesões não medidas" (88) NSA*

14. Tu já tinhas percebido esta ferida **(Lesão 3)** ou machucado na tua boca? Há quanto tempo?

Códigos ##

15. Tu relacionas algum destes sintomas citados a seguir com a tua lesão?

		Lesão 1	
Códigos	*Dor*		*(0) Não*
	Ardência (queimação)		*(0) Não*
	Coceira		*(0) Não*
	Desconforto		*(0) Não*

		Lesão 2	
Códigos	*Dor*		*(0) Não*
	Ardência (queimação)		*(0) Não*
	Coceira		*(0) Não*
	Desconforto		*(0) Não*

		Lesão 3	
Códigos	*Dor*		*(0) Não*
	Ardência (queimação)		*(0) Não*
	Coceira		*(0) Não*
	Desconforto		*(0) Não*

Apêndice F – Nota da Tese

Lesões de mucosa bucal em estudos de base populacional

Oral mucosal lesions in population-based studies

A presente tese de doutorado apresenta os achados de uma extensa busca na literatura científica sobre estudos de base populacional que avaliassem a prevalência de lesões de mucosa bucal, e revela a prevalência desse tipo de lesões em gestantes cujos filhos pertencem a coorte de nascimentos de 2015 de Pelotas, Rio Grande do Sul, Brasil. O objetivo da busca literária foi verificar como os estudos de base populacional sobre prevalência de lesões de mucosa bucal estão sendo conduzidos, ou seja, seus aspectos metodológicos como critérios diagnósticos utilizados, coleta e reporte dos dados. Notou-se falta de padronização das metodologias dos estudos incluídos nessa revisão sistemática. Em relação à análise da ocorrência desse tipo de lesões bucais nas gestantes de Pelotas, observou-se uma prevalência de 16.49%, representada principalmente por alterações bucais que não geram grande prejuízo funcional ou estético para essas mulheres, como exostose, língua saburrosa e pigmentações acastanhadas orais de caráter benigno. Juntos esses resultados auxiliam na condução de novas pesquisa na área, dando suporte ao emprego de metodologias padronizadas, e revelam os primeiros dados que se tem conhecimento sobre lesões de mucosa bucal em gestantes a nível populacional.

Área do Conhecimento do CNPq: Clínica Odontológica

Candidato a Doutor: Karine da Silva, Mestre em Diagnóstico Bucal (2015) e Cirurgiã-Dentista (2014) pela Universidade Federal de Pelotas.

Data da defesa e horário: 09 de julho de 2018 às 15:30.

Local: Auditório do Programa de Pós-graduação em Odontologia da Universidade Federal de Pelotas. 5º andar da Faculdade de Odontologia de Pelotas. Rua Gonçalves Chaves, 457.

Membros da banca: Profa. Dra. Ana Carolina Uchoa Vasconcelos, Profa. Dra. Ana Paula Neutzling Gomes, Profa. Dra. Andréa Homsi Dâmaso, Profa. Dra Adriana Etges (suplente) e Profa. Dra. Fernanda Nedel (suplente).

Orientadora: Profa. Dra. Sandra Beatriz Chaves Tarquinio.
Coorientadores: Prof. Dr. Marcos Britto Correa e Prof. Dr. Flávio Fernando Demarco.
Informação de contato: Karine Duarte da Silva, karineduartedasilva1@gmail.com, Rua Gonçalves Chaves, 457, sala 607 - Centro de Diagnóstico das Doenças da Boca.

Apêndice G– Súmula do currículo do candidato

Súmula do currículo

Karine Duarte da Silva nasceu em 24 de junho de 1987, em Canguçu, Rio Grande do Sul. Completou o ensino médio no Centro Federal de Educação Tecnológica de Pelotas (CEFET/RS). No ano de 2009 efetivamente ingressou na Faculdade de Odontologia da Universidade Federal de Pelotas (FOUFPel), tendo sido graduada cirurgiã-dentista em 2014. No mesmo ano ingressou no Mestrado do Programa de Pós-graduação em Odontologia da Universidade Federal de Pelotas (UFPel), área de concentração Diagnóstico Bucal, sob orientação da Profa. Dra. Sandra Beatriz Chaves Tarquinio. Durante o período de graduação foi bolsista do Programa de Bolsas de Graduação da UFPel (PBG-UFPel) e do Programa Institucional de Bolsas de Iniciação Científica do Conselho Nacional de Desenvolvimento Científico e Tecnológico (PIBIC-CNPq). Durante o período de mestrado foi bolsista da Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (FAPERGS/RS) e realizou estágio no Laboratório de Patologia Experimental I da Faculdade de Odontologia da Universidade Federal de Minas Gerais (FOUFMG). No doutorado foi bolsista da Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) e realizou doutorado-sanduíche no país na FOUFMG. Durante sua pós-graduação desenvolveu trabalhos de cunho epidemiológico e laboratorial relacionados ao carcinoma espinocelular de boca, dentre outras patologias bucais.

Publicações:

Oral Bilateral Collagenous Fibroma: a previously unreported case and review of the literature. Vasconcelos AC, Gomes AP, Tarquinio S, Rodrigues E, Mesquita R, Silva K. Journal of Clinical and Experimental Dentistry, 2018.

Demographic and Clinical Profile of Oral Squamous Cell Carcinoma from a Service-Based Population. Alves A, Correa M, Silva K, Araújo LM, Vasconcelos AC, Gomes AP, Etges A, Traquinio S. Brazilian Dental Journal, 2017.

Características salivares y estado sistémico de sujetos con xerostomía. Saavedra JP, Escobar A, Morales I, Silva K, Parry Y, Olid C. Revista Clínica de Periodoncia, Implantología y Rehabilitación Oral, 2017.

Frequency and histoclinicpathology of malignant and potentially malignant disorders of oral cavity in Chile. Saavedra, JP, Diaz-Valdivia A, Adorno-Farias D, Maturana-Ramirez A, Tarquinio S, Silva K, Fernandez-Ramires R. Journal of Oral Diagnosis, 2017.

Unusual osteolytic lesion of the jaw. Silva K, Flores I, Etges A, Vasconcelos AC, Mesquita R, Gomes AP, Tarquinio S. Oral Surgery Oral Medicine Oral Pathology Oral Radiology, 2017.

Retrospective analysis of jaw biopsies in young adults. A study of 1599 cases in Southern Brazil. Silva K, Alves A, Correa M, Etges A, Vasconcelos AC, Gomes AP, Tarquinio S. Medicina Oral Patologia Oral y Cirugia Bucal, 2017.

Artigos aceitos para publicação:

Salivary flow rate response to stimulation with 2% citric acid in patients with xerostomia. Aitken-Saavedra JP, Munoz R, Rojas-Alcayaga G, Tarquinio S, Silva K, Fernandez-Ramires R, Morales-Bozo I. Journal of Oral Diagnosis, 2018.

High CD3+ lymphocyte, low CD66b+ neutrophil and scarce budding in the invasive front of lip squamous cell carcinoma. Silva K, Caldeira P, Alves A, Vasconcelos AC, Gomes AP, Aguiar MC, Tarquinio S. Medicina Oral Patologia Oral y Cirugia Bucal, 2018.

Anexos

Anexo A – Parecer do Comitê de Ética

FACULDADE DE MEDICINA DA UNIVERSIDADE FEDERAL DE PELOTAS

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: As condições de saúde bucal das mães durante a gravidez podem afetar negativamente os desfechos perinatais? Um estudo em uma coorte de base populacional no Sul do Brasil.

Pesquisador: Flávio Fernando Demarco

Área Temática:

Versão:

CAAE: 31296614.1.0000.5317

Instituição Proponente: Faculdade de Medicina da Universidade Federal de Pelotas

Patrocinador Principal: CNPQ

DADOS DO PARECER
Número do Parecer: 717.271

Data da Relatoria: 29/05/2014

Apresentação do Projeto:

Os estudos com delineamento de coorte prospectiva de nascimentos são atualmente o desenho epidemiológico mais poderoso para investigar as associações entre exposições precoces na vida e desfechos futuros em saúde. Estes estudos suportam a perspectiva do ciclo vital ¿ parte do pressuposto de que o estado de saúde em qualquer idade é o resultado não só de condições atuais, mas também de um acúmulo de condições ao longo da vida. Além disso, a influência de características maternas na saúde do filho vem sendo estabelecida, bem como a relação entre a saúde bucal da mãe e a saúde geral e bucal da criança durante a vida perinatal. Agravos de saúde bucal durante a gravidez podem levar a desfechos de saúde geral adversos, tais como nascimento prematuro e baixo peso ao nascer.

Objetivo da Pesquisa:

Objetivo Primário:

O objetivo geral do presente estudo será avaliar as condições de saúde bucal de todas as gestantes da cidade de Pelotas, parturientes no ano de 2015, cujos filhos serão participantes da Coorte de nascimentos de 2015, a fim de avaliar o impacto das condições de saúde das mães nas condições de saúde das crianças ao nascimento e na infância precoce.

Objetivo Secundário:

Endereço: Rua Prof Araujo, 465 **sala** 301
Bairro: Centro **CEP:** 96.020-360
UF: RS **Município:** PELOTAS
Telefone: (53)3284-4080 **Fax:** (53)3221-3554 **E-mail:** cep.famed@gmail.com