



Is overweight associated with periodontitis in pregnant women? Systematic review and meta-analysis[☆]

Gerson Aparecido Foratori-Junior^{a,b,*}, Priscilla Ramos Pereira^c, Isabella Antunes Gasparoto^c,
Sílvia Helena de Carvalho Sales-Peres^a, Juliana Moura Storniolo de Souza^c, Shahrukh Khan^d

^a Department of Pediatric Dentistry, Orthodontics and Public Health, Bauru School of Dentistry, University of São Paulo, Al. Octávio Pinheiro Brisolla 9-75, 17012-901, Bauru, São Paulo, Brazil

^b Centre for Host-microbiome Interactions, Faculty of Dental, Oral & Craniofacial Sciences, King's College London, SE1 9RT London, UK

^c University of Integrated Faculties of Ourinhos, BR-153 Km 338 S/N, 19909-100, Ourinhos, São Paulo, Brazil

^d Melbourne Dental School, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Grattan St, Melbourne 3010, Victoria, Australia

ARTICLE INFO

Article history:

Received 15 July 2021

Received in revised form 3 December 2021

Accepted 10 January 2022

Available online xxxx

Keywords:

Obesity

Overweight

Periodontitis

Pregnancy

ABSTRACT

This systematic review and meta-analysis aimed to generate pooled evidence for the association between excessive weight and pregnancy induced periodontitis. EMBASE, SCOPUS, PubMed/MEDLINE, Web of Science, BVS/LILACS, Cochrane Library and SCIELO databases were accessed. Eligibility criteria were: human clinical studies published between year 2000 and 2021. Newcastle-Ottawa scale was used to evaluate risk of bias of the studies. Meta-analysis was performed using MedCalc® Statistical Software. Eleven studies were included, evaluating 2152 pregnant women (743 with overweight/obesity and 1409 with normal body mass index - BMI), with a mean age of 29.62 years. Most studies had low risk of bias. A positive association between overweight/obesity and periodontitis was found, with an average of 61.04% of women with overweight/obesity and periodontitis, showing the overall random-effects relative risk and 95% CI of 2.21 (1.53–3.17) ($p < 0.001$). Arterial hypertension, gestational diabetes mellitus and excessive gestational weight gain were the most common adverse effects of maternal obesity that may have been linked to periodontitis induced pro-inflammatory state. In conclusion, a positive association was found between overweight/obesity and periodontitis during pregnancy. However, the high heterogeneity between the studies related to sample size, periodontal classification and the cutoff-points for BMI are the main limitation.

© 2022Published by Elsevier Ltd on behalf of The Japanese Association for Dental Science. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)
CC_BY_NC_ND_4.0

Contents

1. Introduction	42
2. Material and methods	42
2.1. Ethical aspects	42
2.2. Registration of protocol	42
2.3. Search strategy	42
2.4. Eligibility criteria	43
2.5. Data extraction and analysis	43
2.6. Risk of bias (quality) assessment	43
2.7. Meta-analysis	43
3. Results	43

[☆] Scientific field of dental Science: Community dentistry. Periodontology. Pediatric Dentistry.

* Correspondence to: Department of Pediatric Dentistry, Orthodontics and Public Health, Bauru School of Dentistry, University of São Paulo, Bauru, São Paulo, Brazil, Al. Octavio Pinheiro Brisolla, 9-75, Bauru, São Paulo, Brazil.

E-mail address: gerson.foratori@usp.br (G.A. Foratori-Junior).

3.1.	Search results	43
3.2.	Descriptive results	43
3.3.	Measurement of BMI	43
3.4.	Periodontitis examination and classifications	43
3.5.	Covariates	47
3.6.	Quality of included studies	48
3.7.	Sampling methods	48
3.8.	Quantitative results	48
4.	Discussion	48
4.1.	Limitations	50
4.2.	Implications for research	50
4.3.	Implications for practice	50
4.4.	Implication for policy	50
5.	Conclusion	50
	Role of the funding source	50
	Declaration of Competing Interest	50
	References	50

1. Introduction

Several physiological, immunological and hormonal changes occur during pregnancy in order to ensure the woman's body maintenance throughout the gestational period and the development of the fetus [1]. High hormone levels are associated with impaired connective tissue turnover in the periodontium, which may result in an increased inflammatory response in periodontal tissues and, consequently, in an increase in aerobic and anaerobic bacteria and in the higher prevalence of pregnancy-induced periodontal diseases [1].

On the other hand, periodontitis may lead to adverse pregnancy outcomes including pre-term birth and low birth weight of the newborn [2], perinatal mortality [3], gestational diabetes mellitus (GDM) [4] and pre-eclampsia [5]. This occurs as a consequence of profound perturbations in the immune system during pregnancy. Appropriate attention to periodontal health during pregnancy is found to reduce adverse pregnancy outcomes and its effect on maternal and newborn [6]. Research universally supports the safety of dental treatment during pregnancy and confirms that maintaining good oral health prior to and during pregnancy is an important factor in achieving better overall health and well-being for women and their infants [7].

In addition, systemic changes during pregnancy are associated with anemia, maternal weight gain, pregnancy-induced diabetes and arterial hypertension [8–12]. These outcomes are more significant in pregnant women with pre-existing obesity. Obesity represents a major public health challenge because it is related to comorbidities, such as systemic arterial hypertension, diabetes mellitus, obstructive sleep apnea and cancers [13]. Excessive weight is associated with adverse effects in pregnancy such as arterial hypertension, pre-eclampsia, gestational diabetes mellitus, excessive babies' size for gestational age, premature delivery, macrosomia, emergency cesarean section and forced delivery with the aid of instruments [8,14].

Previous evidences demonstrated the association between obesity and periodontitis in the population [15]. The adipose tissue of individuals with obesity secretes inflammatory cytokines and adipokines, which reduce the host's immune response and cause a generalized inflammatory state of body [16]. Therefore, in the presence of biofilm, the individual with obesity may have a more exacerbated inflammatory response of the periodontal tissues. The adverse effects of overweight/obesity in the periodontium can also be mediated by reduced glucose tolerance [17] and dyslipidemia [18].

Based on the rationales that: (i) periodontitis leads to adverse pregnancy outcomes [19,20]; (ii) maternal overweight/obesity is associated with insulin resistance that induces gestational diabetes

mellitus; and (iii) both overweight/obesity and periodontitis are closely linked conditions with pro-inflammatory potential and greater risk to maternal and newborn health, this study aims to investigate the association between overweight/obesity, periodontitis and pregnancy using a systematic review and meta-analysis.

2. Material and methods

The key issue of this systematic review was formulated considering the PI(E)CO strategy: "Is there the association between overweight/obesity and periodontitis in pregnant woman?".

- Population: pregnant women;
- Intervention/Exposure: excessive weight (diagnosis of overweight/obesity);
- Controls: pregnant women with normal BMI;
- Outcome: diagnosis of periodontitis.

2.1. Ethical aspects

This systematic review was conducted without human involvement. Pregnant women were not involved in any way during the review of the available literature, nor during the writing or editing of this document for readability or accuracy.

2.2. Registration of protocol

The search strategy followed the indications of the National Health Service Centre for Reviews and Dissemination and the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines [21]. Also, this systematic review was registered in International Prospective Register of Systematic Reviews (PROSPERO) with protocol CRD42021243782 (<https://www.crd.york.ac.uk/prospero>).

2.3. Search strategy

A systematic revision of relevant studies published in the literature was conducted between April 1st, 2021 to May 05th, 2021, considering the period between January 1st, 2000 to April, 2021. Searches were re-run in May 04th, 2021 prior the final analysis. The following database were explored: BVS/LILACS (<https://www.lilacs.bvsalud.org>); EMBASE (<https://www.embase.com>); SCOPUS (<https://www.scopus.com>); Web of Science (<http://www.isiknowledge.com>); PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>); SCIELO (<https://www.scielo.org/>) and Cochrane Library (<https://www.cochranelibrary.com>), considering the following MeSH (Medical Subject Headings) terms, which were adjusted for each database:

(Pregnancy OR “Pregnant Women” OR “Pregnancy Trimesters” OR “Pregnancy Trimester, Third” OR “Pregnancy Trimester, Second” OR “Pregnancy Trimester, First” OR Pregnant*) AND (“Alveolar Bone Loss” OR Periodontitis OR “Aggressive periodontitis” OR Periodont*) AND (“Body Mass Index” OR “Body Weight” OR Fat OR Overweight OR Obesity OR “Obesity, maternal”).

To identify relevant articles, titles and abstracts of retrieved papers were exported to Endnote Web where duplicates were identified and removed by two reviewers. It is important to highlight that, in order to identify missing studies, we also hand searched the reference lists of the studies included.

2.4. Eligibility criteria

As eligibility criteria, we considered clinical trials, case-control studies, observational studies (cross-sectional and longitudinal studies), in English, Portuguese and Spanish published in peer-reviewed journals, that have addressed the association between excessive weight and periodontitis in female pregnant woman. Duplicate publications and articles that did not correspond to the objectives of this review were excluded. Then, studies non-published, published in grey literature or published with non-pregnant women, pregnant women with cognitive-degenerative impairments and puerperal women were not considered. Similarly, case reports; case series; review articles; descriptive studies; opinion article; correspondence; editorials; and letters were excluded.

2.5. Data extraction and analysis

Two researchers independently conducted the literature search (following the inclusion and exclusion criteria), screening of title, abstract and full text of studies, selection of studies and extraction of data. There was a good concordance coefficient between reviewers (Kappa index = 0.88). Discordances between the authors were discussed and agreed upon with a third author.

Studies assessed in this review were exported to a software system (Endnote Web) where duplicates were identified and removed, afterwards they were classified and stored by: main author, publication year, study design, sample/participants, maternal age, maternal nutritional classification, maternal periodontitis classification, conclusion.

2.6. Risk of bias (quality) assessment

Data heterogeneity and methodological quality of the included studies were assessed using The Newcastle-Ottawa Scale for cohort and case-control studies [22] and Newcastle-Ottawa Scale for cross-sectional studies [23]. The scale is divided in three different sections: study selection; comparability and verification of exposure; and outcome investigated. Questions from each section were analyzed to receive a star/point. According the number of points received, cohort studies were categorized as following: 1) High risk of bias - up to 3 points; 2) Moderate risk of bias - 4–6 points and; 3) Low risk of bias - 7–9 points; and cross-sectional studies were categorized as following: 1) High risk of bias - up to 4 points; 2) Moderate risk of bias - 5–6 points; 3) Low risk of bias - 7–8 points; 4) Very low risk of bias - 9–10 points.

2.7. Meta-analysis

The statistical analyzes were performed using MedCalc® Statistical Software version 19.7.4 (MedCalc Software Ltd, Ostend, Belgium; <https://www.medcalc.org>; 2021). Heterogeneity between the results of the studies included was tested by I^2 statistics. The Mantel-Haenszel type method of Rothman and Boice was used to studies with dichotomous data and relative risk was adopted as

effect measure. A confidence interval for the pooled relative risk is calculated using the Greenland-Robins variance formula. Positive outcomes were considered in the intervention group when data were related to pregnant women with overweight/obesity and periodontitis; and in the control group when data were related to pregnant women with normal BMI and periodontitis. The random effect model was considered for all studies, since, with some different characteristics between the studies, the effect size is expected to be different. Publication bias were examined via Begg's rank correlation.

3. Results

3.1. Search results

The initial search identified 864 studies, being 293 from BVS/LILACS; 155 from EMBASE; 147 from SCOPUS; 92 from Web of Science; 88 from PubMed; 84 from SCIELO and 5 from Cochrane Library. Five hundred and eighty-two sources remained on screening step after duplicates exclusion.

Following screening of titles and abstracts, 556 sources were excluded due to the following reasons: reviews; author reply/comment/ correspondence/ expert comment/ guideline/ letter to editor; not correspond to the objectives of this review; not peer-reviewed; language. Twenty-six articles in full text were assessed. Fifteen were removed due to the following reasons: conference abstract ($n = 6$); did not evaluate the association between overweight/obesity and periodontitis during pregnancy ($n = 8$); and without control group ($n = 1$). Eleven clinical research were considered with good relevance. Fig. 1 shows the steps of the literature search.

3.2. Descriptive results

Table 1 describes the methodology and main findings of the 11 clinical studies included in this review. A total of 2152 pregnant women was considered (743 pregnant women with overweight/obesity and 1409 pregnant women with normal BMI), with a mean age of 29.62 years. Seven studies had a cross-sectional design [25,26,28–30,32,33], whilst two studies were prospective cohort [31,34], one was retrospective cohort [27] and one was a mixed-method study incorporating cross-sectional and case-control designs [24]. The most frequent number of studies were conducted in Brazil ($n = 8$) [24,25,29–34], and others conducted in Korea ($n = 1$) [26], USA ($n = 1$) [27] and Italy ($n = 1$) [28].

3.3. Measurement of BMI

Regarding differences in BMI classifications, Lee et al. [26] defined underweight as $BMI < 18.5 \text{ kg/m}^2$, normal weight as $BMI 18.5–22.9 \text{ kg/m}^2$ and overweight/obesity as $BMI \geq 23 \text{ kg/m}^2$. Overweight also was defined as $BMI 19–25 \text{ kg/m}^2$ and obesity as a $BMI \geq 26 \text{ kg/m}^2$ [24]; Vogt et al. [25] defined obesity as $BMI > 29 \text{ kg/m}^2$. Gomes-Filho et al. [33] adopted an individualized classification according to the gestational week; and the other studies adopted the WHO classification for nutritional status (overweight defined by a $BMI 25–30 \text{ kg/m}^2$ and obesity as $BMI \geq 30 \text{ kg/m}^2$) [27–32,34].

3.4. Periodontitis examination and classifications

Vogt et al. (2012) [25] did not have the examiners' calibration for collection of periodontal data. Piscoya et al. (2012) [24], Zambon et al. (2018) [28], and Gomes-Filho et al. (2020) [33] did not present the reliability coefficient relative to the examiner's calibration.

Many different classifications were adopted: 1) The presence of ≥ 4 teeth that had ≥ 1 sites with probing pocket depth $\geq 4 \text{ mm}$ and clinical attachment loss $\geq 3 \text{ mm}$ at the same site was considered

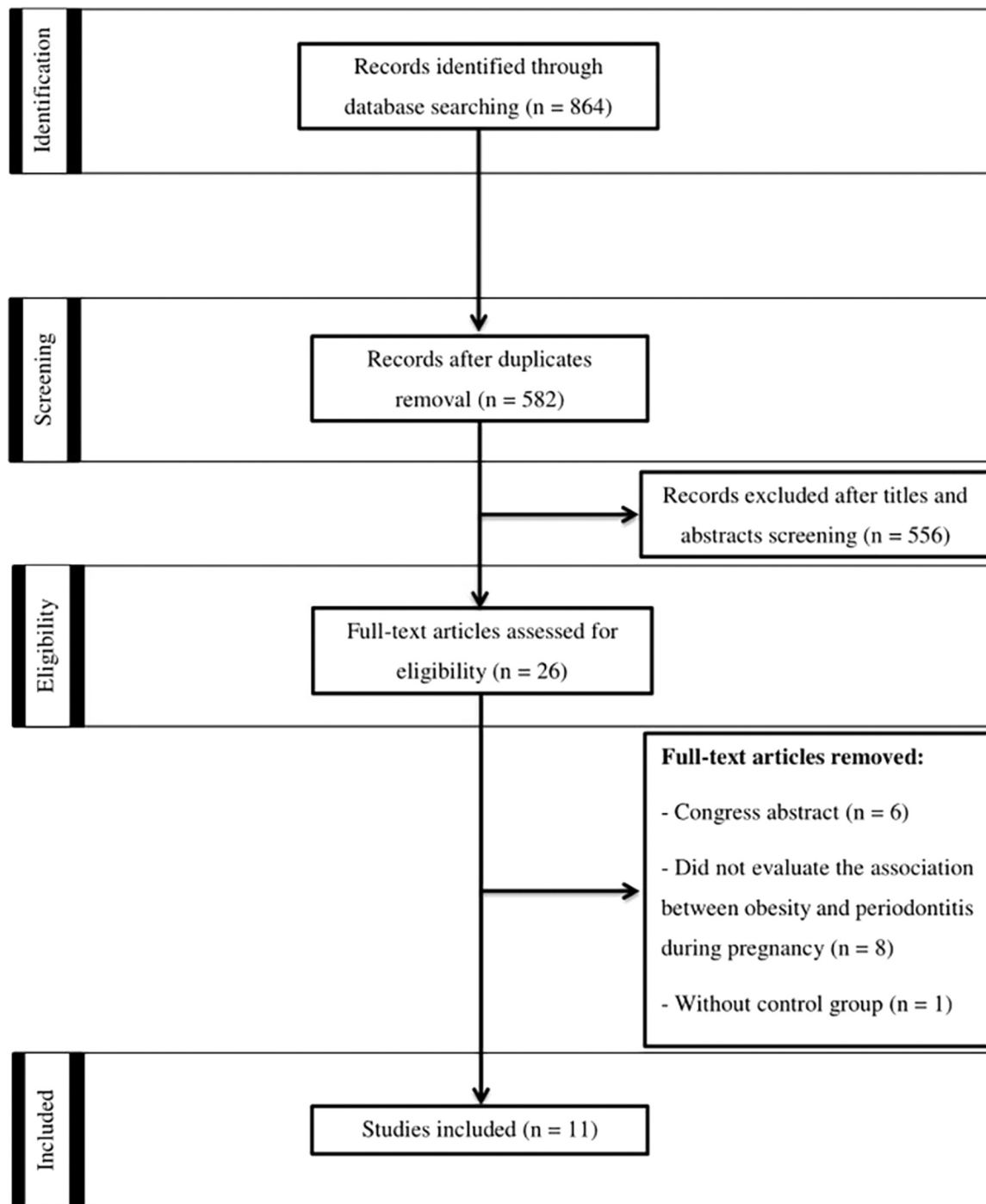


Fig. 1. Flow Diagram of four stages for collection of the study data, highlighting the number of identified, selected, eligible and included studies.

periodontitis [24]. II) Moreover, periodontitis was defined as the presence of ≥ 4 teeth showing ≥ 1 site with ≥ 4 mm of probing pocket depth, clinical attachment loss at the same site, and with bleeding on probing [25]. III) Periodontitis was also defined by the presence of ≥ 2 interproximal sites showing clinical attachment loss ≥ 4 mm that were not on the same tooth [26,31,32], according to definitions from American Academy of Periodontology [35]. IV) An update to those definitions (2012 definitions - American Academy of Periodontology) [36] has also been adopted, in which mild periodontitis was considered when the presence of two or more interproximal sites with clinical attachment loss of ≥ 3 mm (not on the same tooth), or two or more interproximal sites with probing pocket depth of ≥ 4 mm (not on the same tooth), or one site with probing pocket depth of ≥ 5 mm

were found [29,33]. V) Periodontitis classification was also considered by the presence of ≥ 1 sites exhibiting probing pocket depth ≥ 4 mm or clinical attachment loss ≥ 4 mm [27]. VI) Also, periodontitis was defined by probing pocket depth ≥ 4 mm, soft debris, calculus, and bleeding affecting ≥ 6 teeth [28]. VII) Caracho et al. [30] and Foratori-Junior et al. [34] considered that periodontitis was present if interdental clinical attachment loss was detectable on 2 or more nonadjacent teeth or buccal or oral clinical attachment loss of ≥ 3 mm with pocketing of > 3 mm was detectable on 2 or more teeth, and the observed clinical attachment loss was not ascribed to non-periodontal causes. VIII) Finally, Gomes-Filho et al. [33] adopted as mild periodontitis when ≥ 4 teeth present ≥ 1 site with probing

Table 1
Description of selected studies.

Author (year) and country Design	Pregnant women divided according nutritional status	Mean of maternal age	Nutritional classification	Covariates	Periodontitis classification	Conclusions
Piscoya et al. (2012)³⁴ Brazil Cross-sectional/ Case- control	Overweight/obesity (n = 205); Normal BMI (n = 477)	29.50	Excessive: BMI ≥ 26.00 kg/m ² Normal: 19.00–25.00 kg/m ²	Smoking, marital status, schooling, household income, BMI and presence of dental plaque	López, Smith & Gutierrez (2002)	<ul style="list-style-type: none"> - A positive association was found between outcomes. 55.60% of overweight/obese pregnant women had periodontitis (adjusted OR 2.28; 95% CI 1.29–4.02) - Periodontitis during pregnancy was linked with lower schooling level (adjusted OR 4.54; 95% CI 1.62–12.75) and household income (adjusted OR 2.34; 95% CI 1.11–4.94), smoking (adjusted OR 4.17; 95% CI 2.31–7.50), and bacterial plaque (adjusted OR 14.04; 95% CI 3.25–60.64) - Authors suggested positive association between outcomes. 57.14% of overweight/obese pregnant women had periodontitis (PR 1.65; 95% CI 1.02–2.68) - Periodontitis was associated with: more advanced gestational age at the time of the periodontal evaluation (PR 1.52; 95% CI 1.10–2.08), maternal age between 25 and 29 years (PR 1.65; 95% CI 1.02–2.68) and obesity (PR 1.38; 95% CI 1.04–1.82). Being black was at the limit of statistical significance (PR 1.39; 95% CI 1.00–1.94)
Vogt et al. (2012)²⁵ Brazil Cross-sectional	Overweight/obesity (n = 91); Normal BMI (n = 186)	30.50	Excessive: BMI ≥ 26.10 kg/m ² Normal: 19.80–26 kg/m ²	Age, race/color, schooling level, marital status, parity, BMI-estimated with the pre pregnancy weight, systemic disease, smoking, alcohol, drug consumption, medication use, gestational age at examination	López, Smith & Gutierrez (2002)	<ul style="list-style-type: none"> - All 5 Models constructed on obesity and periodontitis association showed a high odds ratio of periodontitis in pregnancy women with overweight/obesity: - Model 1 (OR 4.06; 95% CI 2.15–7.67) adjusted for age only. - Model 2 (OR 4.03; 95% CI 2.15–7.61) adjusted for age at first delivery and parity - Model 3 (OR 4.06; 95% CI 2.29–8.70) adjusted for age, smoking before pregnancy, weekly drinking before pregnancy, weekly exercise before pregnancy - Model 4 (OR 4.15; 95% CI 2.17–7.92) adjusted for Model 3 + use of floss or interdental brush and scaling within 1 year before pregnancy - Model 5 (OR 4.57; 95% CI 2.30–9.07) adjusted for age, age at first delivery and parity, smoking before pregnancy, weekly drinking before pregnancy, weekly exercise before pregnancy, floss or interdental brush use, and scaling within 1 year before pregnancy - Authors suggested positive association between outcomes. 75.80% of overweight/obese pregnant women had periodontitis, with adjusted risk ratios of 1.2 and 1.7 for overweight (adjusted RR 1.2; 95% CI 0.8–1.6) and obesity (adjusted RR 1.6; 95% CI 1.1–2.2), respectively - The covariates adjusted in the model included: age, race, parity, education, marital
Lee et al. (2014)²⁶ Korea Cross-sectional	Overweight/obesity (n = 59); Normal BMI (n = 203)	33.65	Excessive: BMI ≥ 23.00 kg/m ² Normal: 18.50–22.90 kg/m ² (Expert Consultation WHO, 2004)	Smoking, drinking, weekly exercise before pregnancy, floss or interdental brush and scaling within 1 year before pregnancy, parity and age at first delivery	Page & Eke (2007)	
Xie et al. (2014)²⁷ USA Retrospective cohort	Overweight/obesity (n = 86); Normal BMI (n = 73) ^a	28.10	Excessive: BMI ≥ 25.00 kg/m ² Normal: 18.50–24.90 kg/m ² (WHO, 2000)	Maternal age, gestational diabetes mellitus, parity, race, education, family income, marital status, last visit for dental cleaning, frequency of tooth brushing, use of dental floss, mouthrinse, dental or oral disorders treated in pregnancy, and smoking status	Carlos, Wolfe & Kingman (1986)	

(continued on next page)

Table 1 (continued)

Author (year) and country Design	Pregnant women divided according nutritional status	Mean of maternal age	Nutritional classification	Covariates	Periodontitis classification	Conclusions
Zambon et al. (2018)²⁸ Italy Cross-sectional	Obesity (n = 35); Normal BMI (n = 27)	30	Excessive: BMI ≥ 30.00 kg/m ² Normal: 18.50–24.90 kg/m ² (WHO, 2000)	Age, BMI, fasting glycaemia, gestational weight gain, gestational age at delivery, vaginal deliveries, cesarean sections, fetal weight, weight, efficiency, area and thickness of placenta	Page & Eke (2007) with modifications	status, smoking status, stress, dental insurance coverage, oral health behaviors, dental disorder treatment during pregnancy, and last visit for dental cleaning. - Women who had their last dental visit > 12 months ago had slightly higher risk of periodontitis during pregnancy than those with the last dental cleaning occurring 0–12 months ago (RR 1.4; 95% CI 1.1–1.8) - Authors suggested positive association between outcomes. 34.30% of obese pregnant women had periodontitis
Fusco et al. (2019)²⁹ Brazil Cross-sectional	Overweight/obesity (n = 25); Normal BMI (n = 25)	30.70	Excessive: BMI ≥ 25.00 kg/m ² Normal: 18.50–24.90 kg/m ² (WHO, 2000)	Schooling level, monthly household income, presence of gestational diabetes mellitus and arterial hypertension, daily tooth-brushing frequency, daily use of dental floss and regular dental appointments (once per year) before the gestational follow-up	Eke et al. (2012)	- Authors suggested positive association between outcomes. 80% of overweight/obese pregnant women had periodontitis, being moderate (76%) and severe (4%) - During the third trimester, high maternal pre-pregnancy BMI was a significant predictor of arterial hypertension (adjusted OR 1.27; 95% CI 1.03–1.56) and periodontitis (adjusted OR 1.37; 95% CI 1.12–1.67) - Authors suggested positive association between outcomes. 64% of overweight/obese pregnant women had periodontitis (adjusted OR 1.19; 95% CI 1.03–1.36), in stages I (24%) and II (40%). - During the third trimester, high maternal pre-pregnancy BMI was a significant predictor of arterial hypertension (adjusted OR 1.43; 95% CI 1.14–1.79) - Authors suggested positive association between outcomes. 54.71% of overweight/obese pregnant women had moderate periodontitis and 15.10% had severe periodontitis during the 2nd trimester of pregnancy (adjusted OR 1.12; 95% CI 1.01–1.24) - 52.83% of overweight pregnant women had moderate periodontitis and 18.87% were classified as having severe periodontitis during the 3rd trimester of pregnancy (adjusted OR 1.16; 95% CI 1.05–1.29) - Authors suggested positive association between outcomes. 72% of overweight/obese pregnant women had periodontitis (adjusted OR 1.12; 95% CI 1.02–1.21), being moderate (48%) and severe (24%) in all five adjusted binary logistic regression models - No association between outcomes, although 66.67% of overweight/obese pregnant women had periodontitis, being mild (9.52%), moderate (52.38%) and severe (4.76%), (continued on next page)
Caracho et al. (2020)³⁰ Brazil Cross-sectional	Overweight/obesity (n = 25); Normal BMI (n = 25)	27.84	Excessive: BMI ≥ 25.00 kg/m ² Normal: 18.50–24.90 kg/m ² (WHO, 2000)	Maternal BMI, pre-pregnancy BMI, schooling level, monthly household income, gestational arterial hypertension, gestational diabetes mellitus, excessive weight gain, PPD, CAL, calculus, BOP, tooth brushing, flossing, regular dental care by professional, and quality of life (OHIP-14)	Tonetti, Greenwell & Korman (2018)	
Foratori-Junior et al. (2020)³¹ Brazil Prospective cohort	Overweight/obesity (n = 53); Normal BMI (n = 40) They were evaluated both during 2nd and 3rd trimesters of pregnancy	29	Excessive: BMI ≥ 25.00 kg/m ² Normal: 18.50–24.90 kg/m ² (WHO, 2000)	Age, arterial hypertension, diabetes mellitus, BMI 3rd trimester, daily tooth brushing, daily dental flossing, PPD, CAL, dental plaque, BOP	Page & Eke (2007)	
Foratori-Junior et al. (2020)³² Brazil Cross-sectional	Overweight/obesity (n = 50); Normal BMI (n = 50)	29.50	Excessive: BMI ≥ 25.00 kg/m ² Normal: 18.50–24.90 kg/m ² (WHO, 2000)	Maternal age, educational level, monthly household income, arterial hypertension, gestational diabetes mellitus, BMI 3rd trimester, daily tooth brushing, dental floss use, PPD, CAL, and child birth weight	Page & Eke (2007)	
Gomes-Filho et al. (2020)³³ Brazil Cross-sectional	Overweight/obesity (n = 84); Normal BMI (n = 273)	28.50	Individualized according to the gestational week (Atalah et al., 1997)	Age, race, skin color, occupation, schooling level, family income, social class, marital status, household density, smoking habit, alcohol beverage consumption, physical	Eke et al. (2012) Gomes-Filho et al. (2018)	

Table 1 (continued)

Author (year) and country Design	Pregnant women divided according nutritional status	Mean of maternal age	Nutritional classification	Covariates	Periodontitis classification	Conclusions
Foratori-Junior et al. (2021)³⁴ Brazil Prospective cohort	Obesity (n = 30); Normal BMI (n = 30)	29.66	Excessive: BMI ≥ 30.00 kg/m ² Normal: 18.50–24.90 kg/m ² (WHO, 2000)	activity practice, planned pregnancy, number of previous pregnancies, low birth weight child, food and nutritional guidance, guidance on breastfeeding, complications, urinary tract infections, hospital admissions and access to oral health care, dental flossing, tooth brushing, toothache, and presence of dental caries Age, arterial hypertension, diabetes mellitus, BMI 3rd trimester, tooth brushing, dental flossing, PPD, CAL, dental plaque, BOP, and quality of life (OHIP-14)	Tonetti, Greenwell & Korman (2018)	according to Eke et al. (2012) (adjusted PR 0.92; 95% CI 0.62–1.37); and 17.86% of overweight/obese pregnant women had periodontitis, being mild (1.19%), moderate (15.48%) and severe (1.19%), according to Gomes-Filho et al. (2018) (adjusted PR 0.81; 95% CI 0.49–1.40) Authors suggested positive association between outcomes. 73.70% of obese pregnant women had periodontitis (adjusted OR 1.22; 95% CI 1.10–1.38), in stages I (20%), II (26.60%), III (26.60%)

BMI: body mass index; OR: odds-ratio; CI: confidence interval; PR: prevalence ratio; RR: risk ratio.

^a Xie et al. (2014)²⁷ included pregnant women with underweight in the same group with pregnant women with normal BMI, but RR shown in table did not consider pregnant women with underweight.

pocket depth ≥ 4 mm and clinical attachment loss ≥ 1 mm on the same site, also with bleeding upon stimulus.

3.5. Covariates

Piscoya et al. (2012) [24] showed a multivariate model of periodontitis-associated risk factors adjusted by the following covariates: smoking, marital status, schooling, household income, BMI and presence of dental plaque. Overweight/obesity during pregnancy was linked with periodontitis (adjusted OR 2.28; 95% CI 1.29–4.02), as well as, lower schooling level (adjusted OR 4.54; 95% CI 1.62–12.75) and household income (adjusted OR 2.34; 95% CI 1.11–4.94), smoking (adjusted OR 4.17; 95% CI 2.31–7.50), and bacterial plaque (adjusted OR 14.04; 95% CI 3.25–60.64). Vogt et al. (2012) [25] evaluated the following covariates: age, race/color, schooling level, marital status, parity, BMI-estimated with the pre pregnancy weight, systemic disease, smoking, alcohol, drug consumption, medication use, gestational age at examination. Periodontitis was associated with: more advanced gestational age at the time of the periodontal evaluation (PR 1.52; 95% CI 1.10–2.08), maternal age between 25 and 29 years (PR 1.65; 95% CI 1.02–2.68) and obesity (PR 1.38; 95% CI 1.04–1.82). Being black was at the limit of statistical significance (PR 1.39; 95% CI 1.00–1.94).

Covariates assessed by Lee et al. (2014) [26] were: smoking, drinking, weekly exercise before pregnancy, floss or interdental brush and scaling within 1 year before pregnancy, parity and age at first delivery. When adjusted for all variables, females who were overweight/obese before pregnancy were 4.6 times more likely to have periodontitis than normal-weight females (OR 4.57; 95% CI 2.30–9.07). The covariates adjusted in the model of Xie et al. (2014) [27] included: age, race, parity, education, marital status, smoking status, stress, dental insurance coverage, oral health behaviors, dental disorder treatment during pregnancy, and last visit for dental cleaning. Overweight/obese pregnant women had higher risk for periodontitis, with adjusted risk ratios of 1.2 and 1.7 for overweight (adjusted RR 1.2, 95% CI 0.8–1.6) and obesity (adjusted RR 1.6, 95% CI 1.1–2.2), respectively. Zamboni et al. (2018) [28] assessed maternal age, BMI, fasting glycaemia, gestational weight gain (GWG), gestational age at delivery, vaginal deliveries, cesarean sections, fetal weight, weight, efficiency, area and thickness of placenta.

Fusco et al. (2019) [29] showed that high maternal pre-pregnancy BMI was a significant predictor of arterial hypertension (adjusted OR 1.27; 95% CI 1.03–1.56) and periodontitis (adjusted OR 1.37; 95% CI 1.12–1.67). The covariates assessed were: schooling level, monthly household income, presence of gestational diabetes mellitus and arterial hypertension, daily tooth-brushing frequency, daily use of dental floss and regular dental appointments (once per year) before the gestational follow-up. In the same way, Caracho et al. (2020) [30] evaluated maternal BMI, pre-pregnancy BMI, schooling level, monthly household income, gestational arterial hypertension, gestational diabetes mellitus, excessive weight gain, PPD, CAL, calculus, BOP, tooth brushing, flossing, regular dental care by professional. They highlighted that high pre-pregnancy BMI was associated with both arterial hypertension during pregnancy (OR 1.43; 95% CI 1.14–1.79) and periodontitis (OR 1.19; 95% CI 1.03–1.36).

Foratori-Junior et al. (2020) [31,32] and Foratori-Junior et al. (2021) [34] assessed maternal age, educational level, monthly household income, arterial hypertension, gestational diabetes mellitus, BMI 3rd trimester, daily tooth brushing, dental floss use, PPD and CAL. Foratori-Junior et al. (2020) [31] showed that in the final logistic regression model adjusted by maternal age, household monthly income, maternal BMI and hypertension during the third trimester of pregnancy, high BMI was associated with periodontitis (adjusted OR 1.16; 95% CI 1.05–1.29). In the same way, Foratori-Junior et al. (2020) [32] adjusted the model by pre-pregnancy BMI, educational level, and hypertension and diabetes mellitus, showing

Table 2

Scores from Newcastle-Ottawa scale (versions for cohort and cross-sectional studies).

Authors (year)	Items				Risk of bias	Outcomes association
	Selection	Comparability	Outcome	Score		
Piscoya et al. (2012) ²⁴	●●●●	●●	●●●	9	Very low	Yes
Vogt et al. (2012) ²⁵	●●●	●	●●●	7	Low	Yes
Lee et al. (2014) ²⁶	●●●	●●	●●●	8	Low	Yes
Xie et al. (2014) ²⁷	●●●	●●	●●	7	Low	Yes
Zambom et al. (2018) ²⁸	●●	●●	●●●	7	Low	Yes
Fusco et al. (2019) ²⁹	●	●●	●●●	6	Moderate	Yes
Caracho et al. (2020) ³⁰	●●	●●	●●●	7	Low	Yes
Foratori-Junior et al. (2020) ³¹	●●●	●●	●●●	8	Low	Yes
Foratori-Junior et al. (2020) ³²	●●●	●●	●●●	8	Low	Yes
Gomes-Filho et al. (2020) ³³	●●●●	●●	●●●	9	Very low	No
Foratori-Junior et al. (2021) ³⁴	●●	●●	●●●	7	Low	Yes

association of high BMI with periodontitis (adjusted OR 1.12; 95% CI 1.02–1.21). When adjusted for dental plaque, hypertension, and maternal BMI, Foratori-Junior et al. (2021) [34] also demonstrated that pregnant women with overweight/obesity are more prone to periodontitis (adjusted OR 1.22; 95% CI 1.10–1.38).

Gomes-Filho et al. (2020) [33] evaluated: age, race, skin color, occupation, schooling level, family income, social class, marital status, household density, smoking habit, alcohol beverage consumption, physical activity practice, planned pregnancy, number of previous pregnancies, low birth weight child, food and nutritional guidance, guidance on breastfeeding, complications, urinary tract infections, hospital admissions and access to oral health care, dental flossing, tooth brushing, toothache, and presence of dental caries. The following covariables presented statistically significant differences: age, number of previous pregnancies, smoking, food and nutritional orientation, alcoholic beverage consumption, number of prenatal consultations, and arterial hypertension as a complication of the current gestation. They did not find association between overweight/obesity and periodontitis, neither according to Eke et al. (2012) classification (adjusted PR 0.92; 95% CI 0.62–1.37), nor Gomes-Filho et al. (2018) classification (adjusted PR 0.81; 95% CI 0.49–1.40).

3.6. Quality of included studies

According to the Newcastle–Ottawa Scale for cohort studies and the modified Newcastle–Ottawa Scale for cross-sectional studies, the risk of bias was considered very low [24,33], low [25–28,30–32,34] and moderate [29], as demonstrated in Table 2. Excluding Fusco et al. (2019) [29], all other studies had a low risk of bias. Fusco et al. (2019) [29] presented moderate risk, whilst Piscoya et al. (2012) [24] and Gomes-Filho et al. (2020) [33] presented very low risk of bias (Table 2). The selection methods, mainly related to the representativeness of the sample and the justification for calculating the sample size were the main factors for the study of Fusco et al. (2019) to be classified as having a moderate risk of bias.

3.7. Sampling methods

It is important to point out that all the included studies involved a convenience non-randomized sample. Vogt et al. (2012) [25], Lee et al. (2014) [26], and Zambom et al. (2018) [28] did not justify the sample size of their studies. Xie et al. (2014) [27], Zambom et al. (2018) [28], Fusco et al. (2019) [29], Caracho et al. (2020) [30], Foratori-Junior et al. (2020) [31,32], and Foratori-Junior et al. (2021) [34] presented the sample size as limitation of the study. Piscoya et al. (2012) [24], Vogt et al. (2012) [25], Lee et al. (2014) [26], and Gomes-Filho et al. (2020) [33] had the largest samples.

3.8. Quantitative results

All studies were included in dichotomous meta-analysis since all of them showed the number of participants with events (periodontitis) and total number of participants in experimental (overweight/obesity) and control groups (normal BMI) ($n = 11$). RR of periodontitis, 95% CI and weight of the association for each result are demonstrated in Fig. 2.

For the association between prevalence of periodontitis and overweight/obesity in pregnant women, the overall random-effects RR and 95% CI was 2.21 (1.53–3.17) with a χ^2 statistic for heterogeneity (Q) of 88.88 with 10 degrees of freedom ($p < 0.0001$), showing high heterogeneity between the studies (88.75%). Despite the heterogeneity, the RR of periodontitis in overweight/obesity group was statistically significant ($p < 0.001$). Fig. 2 depicts the forest plot as a graphical representation of the individual results that contributed to meta-analysis. The result revealed that Begg's test ($p = 0.073$) did not indicate any evidence of publication bias.

Only one [33] among the 11 studies included in the systematic review did not find an association between periodontitis and overweight/obesity in pregnant women. However, in that study, the authors indicated as limitation the gestational age of the participants at the time of assessment of their oral condition, since most participants were examined in their first trimester [33]. Possibly, if the oral evaluation had been performed in the last gestational trimester, the authors could have found a positive association between outcomes.

4. Discussion

This present meta-analysis contributes to the scientific evidence since it clarifies the association between periodontitis and overweight/obesity during pregnancy. The main barriers that hinder the understanding of the association of these outcomes are: divergences between studies regarding the sample size, the classification of periodontitis and nutritional status (cut-off point of BMI).

Despite high heterogeneity between the studies (88.75%; $Q = 88.88$, $df = 10$; $p < 0.0001$), meta-analysis suggests a significantly positive association between overweight/obesity and periodontitis during pregnancy (RR = 2.21; 95% IC = 1.53–3.17; $p < 0.001$).

Overweight/obesity is known to trigger a generalized inflammatory response in the body of individuals due to the production of pro-inflammatory cytokines (IL-1, IL-6, IL-8 and TNF- α), adipokines (leptin, adiponectin, resistin and inhibitors of plasminogen activator-1) and other bioactive substances, such as reactive oxygen species, by adipose tissue. The impairment of the immune response of the individual with overweight/obesity is due to changes in T lymphocytes and monocytes/macrophages. Faced with this, individuals become more prone to inflammation in the oral cavity, even in the presence of a small amount of plaque. Previous evidences

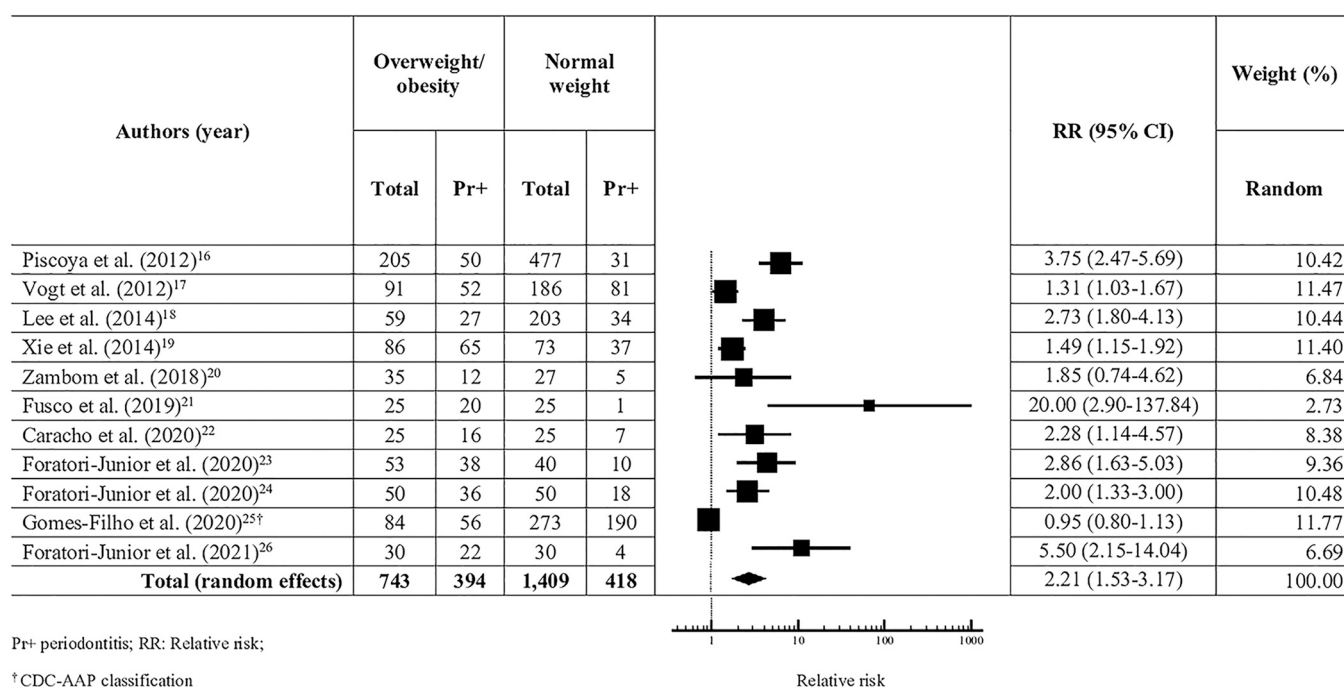


Fig. 2. Meta-analysis forest plot. The forest plot is a graphical depiction of the individual results that contributed to meta-analysis. Sizes of the boxes are proportional to the weight assigned to each result in calculating the random-effects relative risk (RR).

have highlighted the direct mechanism of obesity to an increased inflammatory response to plaque in the oral cavity [16–19,37–40].

Several hypotheses for biological interactions between pregnancy and periodontal diseases have been proposed, such as: reduction of the antimicrobial activity of peripheral neutrophils, increase in the proportion of aerobic and anaerobic bacteria (*Bacteroides melaninogenicus*, *Prevotella intermedia* and *Porphyromonas gingivalis*), changes in the periodontal connective tissue turnover and high levels of estrogen and progesterone [1]. It is hypothesized that these biological interactions during pregnancy become more intense when there is an association with the immunological damage resulting from overweight/obesity.

Social Determinants of Health are specific characteristics of the social context that can affect individual health through social conditions, such as income, education, occupation, family structure, availability of services, sanitation, exposure to diseases, networks and social support, social discrimination and access to preventive health actions [41]. Age, socioeconomic status, oral hygiene habits, smoking, diabetes mellitus, blood pressure and gestational weight gain are important co-variables assessed in the association between overweight/obesity and periodontitis.

This study indicated that pregnant women with overweight/obesity have demonstrated lower income [27,31,32], education level [31,32], poor oral hygiene [28], high prevalence of arterial hypertension [28–34] and gestational diabetes mellitus [27,28,31,32], and presented lower dental assistance during pregnancy [27,29,30,33]. Xie et al. [27] pointed out a higher prevalence of pregnant women of African American descent having overweight/obesity and periodontitis. Lee et al. [26] and Caracho et al. [30] highlighted that the pregnant women with overweight/obesity, who also had a higher prevalence of periodontitis, were older.

The association of overweight/obesity and periodontitis with lower socioeconomic status can be explained by the fact that individuals with lower socioeconomic status show inadequate eating behaviors due to their reliance on low cost food products that often have high caloric value and lower nutrition content, resulting in greater risk for weight gain [31,32]. Likewise, individuals with lower socioeconomic status have impaired access to health services and

dental care services, reduced oral hygiene care knowledge, and greater risk of preventable hospital admission [42].

Gestational diabetes mellitus results from a reduction in pancreatic β -cell function, consequently, there is a reduction in carbohydrate metabolism, requiring an increase in insulin levels [12]. There is a triangular relationship between overweight/obesity, gestational diabetes mellitus and periodontitis. It is believed that both periodontitis and overweight/obesity are capable of inducing local and host immune responses causing both transient bacteremia and the release of inflammatory markers such as interleukins and tumor necrosis factors, which then can act multiplicatively to block the effect and action of insulin, or act via the destruction of pancreatic beta cells to prevent its production. This process consequently leads to insulin resistance and impairment of glucose metabolism and, if not reversed, to gestational diabetes mellitus [43].

Hypertension, in turn, is related to the vascular inflammation and endothelial disturbance. Inflammatory cytokines and adipokines increase the vascular permeability and promote cytoskeletal changes in the endothelial cells, which can disrupt the balance between vasodilation and vasoconstriction. The widespread inflammation resulting from overweight/obesity makes vasoconstriction more intense. Elevated gestational hormone levels may play a key role in this mechanism and clinically it is diagnosed as arterial hypertension [32,44,45]. There are evidences that associate periodontitis with arterial hypertension, also due to the changes in the hosts' pro-inflammatory and immune response. However, the causal direction of these outcomes is unclear [46].

Besides maternal obesity, studies indicate that excessive gestational weight gain is also associated with several complications, such as GDM, hypertension, pre-eclampsia, emergency cesarean section, premature and stillbirth and spontaneous abortion [11,47,48]. The biological interactions of the individual with obesity aforementioned are similar for pregnant women with excessive gestational weight gain. High macronutrients intake is associated with the accumulation of lipids in adipocytes and expansion of adipose tissue, which may initiate an inflammatory process through the production of pro-inflammatory cytokines and chemokines, such as the tumor necrosis factor alpha (TNF- α), interleukin 6 (IL-6) and C-reactive protein

(CRP), by adipocytes [20,27,38,39,49,50]. Jesuino et al. (2020) highlighted that pregnant women with excessive GWG have a high prevalence of hypertension and periodontitis, with periodontitis persisting even after delivery. Furthermore, excessive GWG was significantly associated with high BMI of newborns [50].

4.1. Limitations

This study has some limitations. The small number of studies included in the meta-analysis favors the presence of publication bias, however the Begg's test did not reveal a statistically significant publication bias ($p=0.073$). In addition, the studies showed great variation in the sample size, which, added to the divergences in the parameters of classification of nutritional status and periodontitis, result in high heterogeneity of the studies, making it difficult to compare them in order to understand the association of the outcomes. Finally, for a better understanding of the association of outcomes, population-based prospective cohorts should be conducted and should assess women in the same gestational period, with preference for the third trimester of pregnancy, since greater hormonal changes are expected in that period.

4.2. Implications for research

The evidence generated from this systematic review are guiding principles towards use of robust standardized definitions and classification models for periodontitis, body composition measures, social demographic variables, health service use data, and risk behaviour data across the studies. This would lead to much clearer comparison for the studies across varying cohorts and will generate meaningful outputs. Future research should adopt longitudinal prospective cohort study design and must utilize robust statistical models that leads to understanding of life course mechanics of maternal oral health and general health, and its rudimentary effect on child health. It is essential that future studies assess the progression of inflammation in periodontal tissues over the gestational trimesters, as in this review only one study evaluated women at different times of pregnancy. Furthermore, the only study that did not find an association between the outcomes evaluated pregnant women in early pregnancy and, possibly, the association between periodontitis and overweight/obesity could have been elucidated if women had been evaluated in the third trimester, when there are higher hormone levels.

4.3. Implications for practice

In view of the outputs of this systematic review and meta-analysis, we highlight that there is a need for an oral health care tool kit development that should be used by allied health professionals in oral health care promotion as part of their midwifery and obstetric practice. In addition, regular 12-monthly visit to a dentist promotion should be part of routine practice to embed a habit of dental visiting among mothers and subsequently among their children.

4.4. Implication for policy

New policies must be devised that works on lifespan health model with aims to achieve universal health coverage for all, and towards development of generation that receive equitable health care and dental care services.

5. Conclusion

Despite the limitations, this study contributes to the scientific literature. Considering that previous evidences have associated maternal periodontitis with worse baby health parameters [51,52],

such as prematurity and low birth weight, understanding the association between overweight/obesity and periodontitis during pregnancy is essential for protocols for the care of women to be adopted during pregnancy, in order to ensure better health conditions for women and babies. The results of the present systematic review provide evidence that there is an association between overweight/obesity and periodontitis during pregnancy. Nonetheless, the heterogeneity of the studies regarding sample size, classification of maternal nutritional status and periodontitis is the main limitation.

Role of the funding source

This work was supported by the Coordination of Superior Level Staff Improvement (CAPES) - Brazil (Financial code 001); and the São Paulo Research Foundation (FAPESP) - Brazil (scholarship grant #2018/20626-5). CAPES and FAPESP had no role in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

Declaration of Competing Interest

Authors declare no conflict of interest.

References

- [1] Silva de Araujo Figueiredo C, Gonçalves Carvalho Rosalem C, Costa Cantanhede AL, Abreu Fonseca Thomaz ÉB, Fontoura Nogueira da Cruz MC. Systemic alterations and their oral manifestations in pregnant women. *J Obstet Gynaecol Res* 2017;43:16–22. <https://doi.org/10.1111/jog.13150>
- [2] Pozo E, Mesa F, Ikram MH, Puertas A, Torrecillas-Martínez L, Ortega-Oller I, et al. Preterm birth and/or low birth weight are associated with periodontal disease and the increased placental immunohistochemical expression of inflammatory markers. *Histol Histopathol* 2016;31:231–7. <https://doi.org/10.14670/HH-11-671>
- [3] Shub A, Wong C, Jennings B, Swain JR, Newnham JP. Maternal periodontal disease and perinatal mortality. *Aust N Z J Obstet Gynaecol* 2009;49:130–6. <https://doi.org/10.1111/j.1479-828x.2009.00953.x>
- [4] Kumar A, Sharma DS, Verma M, Lamba AK, Gupta MM, Sharma S, et al. Association between periodontal disease and gestational diabetes mellitus (GDM)—a prospective cohort study. *J Clin Periodontol* 2018;45:920–31. <https://doi.org/10.1111/jcpe.12902>
- [5] Kunnen A, van Doormaal JJ, Abbas F, Aarnoudse JG, van Pampus MG, Faas MM. Periodontal disease and pre-eclampsia: a systematic review. *J Clin Periodontol* 2010;37:1075–87. <https://doi.org/10.1111/j.1600-051X.2010.01636.x>
- [6] George A, Shamim S, Johnson M, Ajwani S, Bhole S, Blinkhorn A, et al. Periodontal treatment during pregnancy and birth outcomes: a meta-analysis of randomised trials. *Int J Evid Based Health* 2011;9:122–47. <https://doi.org/10.1111/j.1744-1609.2011.00210.x>
- [7] Dasanayake AP, Gennaro S, Hendricks-Muñoz KD, Chhun N. Maternal periodontal disease, pregnancy, and neonatal outcomes. *MCN Am J Matern Child Nurs* 2008;33:45–9. <https://doi.org/10.1097/01.NMC.0000305657.24613.47>
- [8] Catalano PM, Shankar K. Obesity and pregnancy: mechanisms of short term and long term adverse consequences for mother and child. *BMJ* 2017;356:j1. <https://doi.org/10.1136/bmj.j1>
- [9] Smith C, Teng F, Branch E, Chu S, Joseph KS. Maternal and perinatal morbidity and mortality associated with anemia in pregnancy. *Obstet Gynecol* 2019;134:1234–44. <https://doi.org/10.1097/AOG.0000000000003557>
- [10] Agrawal A, Wenger NK. Hypertension during pregnancy. *Curr Hypertens Rep* 2020;22:64. <https://doi.org/10.1007/s11906-020-01070-0>
- [11] Champion ML, Harper LM. Gestational weight gain: update on outcomes and interventions. *Curr Diab Rep* 2020;20:11. <https://doi.org/10.1007/s11892-020-1296-1>
- [12] Oskovi-Kaplan ZA, Ozgu-Erdinc AS. Management of gestational diabetes mellitus. *Adv Exp Med Biol* 2021;1307:257–72. https://doi.org/10.1007/5584_2020_552
- [13] Blüher M. Obesity: global epidemiology and pathogenesis. *Nat Rev Endocrinol* 2019;15:288–98. <https://doi.org/10.1038/s41574-019-0176-8>
- [14] Lindberger E, Sundström Poromaa I, Ahlsson F. Impact of maternal central adiposity on infant anthropometry and perinatal morbidity: a systematic review. *Eur J Obstet Gynecol Reprod Biol* 2020;8:100117. <https://doi.org/10.1016/j.eurox.2020.100117>
- [15] Martínez-Herrera M, Silvestre-Rangil J, Silvestre FJ. Association between obesity and periodontal disease. A systematic review of epidemiological studies and controlled clinical trials. *Med Oral Patol Oral Cir Bucal* 2017;22:e708–15. <https://doi.org/10.4317/medoral.21786>
- [16] Coppack SW. Pro-inflammatory cytokines and adipose tissue. *Proc Nutr Soc* 2001;60:349–56. <https://doi.org/10.1079/pns2001110>
- [17] Saito T, Shimazaki Y, Kiyohara Y, Kato I, Kubo M, Iida M, et al. Relationship between obesity, glucose tolerance, and periodontal disease in Japanese women: the Hisayama study. *J Periodontol Res* 2005;40:346–53. <https://doi.org/10.1111/j.1600-0765.2005.00813.x>

- [18] Saito T, Shimazaki Y. Metabolic disorders related to obesity and periodontal disease. *Periodontol* 2000 2007;43:254–66. <https://doi.org/10.1111/j.1600-0757.2006.00186.x>
- [19] Khan S, Barrington G, Bettiol S, Barnett T, Crocombe L. Is overweight/obesity a risk factor for periodontitis in young adults and adolescents?: a systematic review. *Obes Rev* 2018;19:852–83. <https://doi.org/10.1111/obr.12668>
- [20] Khan S, Bettiol S, Kent K, Barnett T, Peres M, Crocombe LA. Obesity and periodontitis in Australian adults: a population-based cross-sectional study. *Int Dent J* 2020;70:53–61. <https://doi.org/10.1111/idj.12514>
- [21] Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;283:2008–12. <https://doi.org/10.1001/jama.283.15.2008>
- [22] Wells GA, Shea B., O'Connell D., Peterson J., Welch V., Losos M., et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. Department of Epidemiology and Community Medicine, University of Ottawa, Canada. Available at: www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
- [23] Ferreira MC, Dias-Pereira AC, Branco-de-Almeida LS, Martins CC, Paiva SM. Impact of periodontal disease on quality of life: a systematic review. *J Periodontol Res* 2017;52:651–65. <https://doi.org/10.1111/jre.12436>
- [24] Piscioya MD, Ximenes RA, Silva GM, Jamelli SR, Coutinho SB. Periodontitis-associated risk factors in pregnant women. *Clinics (Sao Paulo)* 2012;67:27–33. [https://doi.org/10.6061/clinics/2012\(01\)05](https://doi.org/10.6061/clinics/2012(01)05)
- [25] Vogt M, Sallum AW, Cecatti JG, Morais SS. Factors associated with the prevalence of periodontal disease in low-risk pregnant women. *Reprod Health* 2012;9:3. <https://doi.org/10.1186/1742-4755-9-3>
- [26] Lee HJ, Jun JK, Lee SM, Ha JE, Paik DI, Bae KH. Association between obesity and periodontitis in pregnant females. *J Periodontol* 2014;85:e224–31. <https://doi.org/10.1902/jop.2014.130578>
- [27] Xie Y, Xiong X, Elkind-Hirsch KE, Pridjian G, Maney P, Delarosa RL, et al. Prepregnancy obesity and periodontitis among pregnant females with and without gestational diabetes mellitus. *J Periodontol* 2014;85:890–8. <https://doi.org/10.1902/jop.2013.130502>
- [28] Zambon M, Mandò C, Lissoni A, Anelli GM, Novielli C, Cardellicchio M, et al. Inflammatory and oxidative responses in pregnancies with obesity and periodontal disease. *Reprod Sci* 2018;25:1474–84. <https://doi.org/10.1177/1933719117749758>
- [29] Fusco NDS, Foratori-Junior GA, Missio ALT, Jesuino BG, Sales-Peres SHC. Systemic and oral conditions of pregnant women with excessive weight assisted in a private health system. *Int Dent J* 2019;69:472–9. <https://doi.org/10.1111/idj.12507>
- [30] Caracho RA, Foratori-Junior GA, Fusco NDS, Jesuino BG, Missio ALT, Sales-Peres SHC. Systemic conditions and oral health-related quality of life of pregnant women of normal weight and who are overweight. *Int Dent J* 2020;70:287–95. <https://doi.org/10.1111/idj.12547>
- [31] Foratori-Junior GA, da Silva BM, da Silva Pinto AC, Honório HM, Groppo FC, de Carvalho Sales-Peres SH. Systemic and periodontal conditions of overweight/obese patients during pregnancy and after delivery: a prospective cohort. *Clin Oral Investig* 2020;24:157–65. <https://doi.org/10.1007/s00784-019-02932-x>
- [32] Foratori-Junior GA, Jesuino BG, Caracho RA, Orenha ES, Groppo FC, Sales-Peres SHC. Association between excessive maternal weight, periodontitis during the third trimester of pregnancy, and infants' health at birth. *J Appl Oral Sci* 2020;28:e20190351 <https://doi.org/10.1590/1678-7757-2019-0351>
- [33] Gomes-Filho IS, Batista JET, Trindade SC, Passos-Soares JS, Cerqueira EMM, Costa TSD, et al. Obesity and periodontitis are not associated in pregnant women. *J Periodontol Res* 2020;55:77–84. <https://doi.org/10.1111/jre.12690>
- [34] Foratori-Junior GA, Missio ALT, Orenha ES, de Carvalho Sales-Peres SH. Systemic condition, periodontal status, and quality of life in obese women during pregnancy and after delivery. *Int Dent J* 2021. <https://doi.org/10.1016/j.identj.2020.12.012>
- [35] Page RC, Eke PI. Case definitions for use in population-based surveillance of periodontitis. *J Periodontol* 2007;78:1387–99. <https://doi.org/10.1902/jop.2007.060264>
- [36] Eke PI, Page RC, Wei L, Thornton-Evans G, Genco RJ. Update of the case definitions for population-based surveillance of periodontitis. *J Periodontol* 2012;83:1449–54. <https://doi.org/10.1902/jop.2012.110664>
- [37] Furugen R, Hayashida H, Kitamura M, Saito T. Relationship between adipokines and periodontitis. *Jpn Dent Sci Rev* 2010;46:159–64. <https://doi.org/10.1016/j.jdsr.2010.01.001>
- [38] Moura-Grec PG, Marsicano JA, Carvalho CA, Sales-Peres SH. Obesity and periodontitis: systematic review and meta-analysis. *Cien Saude Colet* 2014;19:1763–72. <https://doi.org/10.1590/1413-81232014196.13482013>
- [39] Keller A, Rohde JF, Raymond K, Heitmann BL. Association between periodontal disease and overweight and obesity: a systematic review. *J Periodontol* 2015;86:766–76. <https://doi.org/10.1902/jop.2015.140589>
- [40] Martens L, De Smet S, Yusuf MY, Rajasekharan S. Association between overweight/obesity and periodontal disease in children and adolescents: a systematic review and meta-analysis. *Eur Arch Paediatr Dent* 2017;18:69–82. <https://doi.org/10.1007/s40368-017-0272-1>
- [41] Wang E, Glazer KB, Howell EA, Janevic TM. Social determinants of pregnancy-related mortality and morbidity in the United States: a systematic review. *Obstet Gynecol* 2020;135:896–915. <https://doi.org/10.1097/AOG.0000000000003762>
- [42] Crocombe LA, Allen P, Bettiol S, Khan S, Godwin D, Barnett T, et al. Geographical variation in preventable hospital admissions for dental conditions: an Australia-wide analysis. *Aust J Rural Health* 2019;27:520–6. <https://doi.org/10.1111/ajr.12556>
- [43] Abariga SA, Whitcomb BW. Periodontitis and gestational diabetes mellitus: a systematic review and meta-analysis of observational studies. *BMC Pregnancy Childbirth* 2016;16:344. <https://doi.org/10.1186/s12884-016-1145-z>
- [44] Izumi Y, Nagasawa T, Umeda M, Kobayashi H, Takeuchi Y, Yashiro R, et al. Periodontitis and cardiovascular diseases: the link and relevant mechanisms. *Jpn Dent Sci Rev* 2009;45:98–108. <https://doi.org/10.1016/j.jdsr.2009.06.001>
- [45] Macedo Paizan ML, Vilela-Martin JF. Is there an association between periodontitis and hypertension? *Curr Cardiol Rev* 2014;10:355–61. <https://doi.org/10.2174/1573403x10666140416094901>
- [46] Muñoz Aguilera E, Suvar J, Buti J, Czesnikiewicz-Guzik M, Barbosa Ribeiro A, Orlandi M, et al. Periodontitis is associated with hypertension: a systematic review and meta-analysis. *Cardiovasc Res* 2020;116:28–39. <https://doi.org/10.1093/cvr/cvz201>
- [47] LifeCycle Project-Maternal Obesity, Childhood Outcomes Study Group, Voerman E, Santos S, Inskip H, Amiano P. Association of gestational weight gain with adverse maternal and infant outcomes. *JAMA* 2019;321:1702–15. <https://doi.org/10.1001/jama.2019.3820>
- [48] Blau LE, Hormes JM. Preventing excess gestational weight gain and obesity in pregnancy: the potential of targeting psychological mechanisms. *Curr Obes Rep* 2020;9:522–9. <https://doi.org/10.1007/s13679-020-00415-9>
- [49] Zimmermann GS, Bastos MF, Dias Gonçalves TE, Chambrone L, Duarte PM. Local and circulating levels of adipocytokines in obese and normal weight individuals with chronic periodontitis. *J Periodontol* 2013;84:624–33. <https://doi.org/10.1902/jop.2012.120254>
- [50] Jesuino BG, Foratori-Junior GA, Missio ALT, Mascoli LS, Sales-Peres SHC. Periodontal status of women with excessive gestational weight gain and the association with their newborns' health. *Int Dent J* 2020;70:396–404. <https://doi.org/10.1111/idj.12580>
- [51] Manrique-Corredor EJ, Orozco-Beltran D, Lopez-Pineda A, Quesada JA, Gil-Guillen VF, Carratala-Munuera C. Maternal periodontitis and preterm birth: systematic review and meta-analysis. *Community Dent Oral Epidemiol* 2019;47:243–51. <https://doi.org/10.1111/cdoe.12450>
- [52] Figuero E, Han YW, Furuichi Y. Periodontal diseases and adverse pregnancy outcomes: mechanisms. *Periodontol* 2000 2020;83:175–88. <https://doi.org/10.1111/prd.12295>