

Impact of maternal periodontitis on preterm birth and low birth weight in babies: results of a scoping review

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Abstract

Background : World wide, numerous studies have shown a significant association between periodontitis and prematurity and/ or low birth weight particularly in developing countries. Periodontitis has been documented as public health concern but its association with preterm and /or low birth weight remains uncertain, thus the objective of this scoping review is to summarize the most recent published evidence related to the effect of periodontitis on preterm birth and low birth weight.

Methods Hinari, PubMed, and Google Scholar were searched to acquire the published literature. The retrieved studies included cross-sectional, case control studies and randomized controlled trials with available full text published in English from 2008 to 2019. The key words used to identify relevant articles for review included the following: periodontitis, periodontal disease, pregnancy, preterm birth, and low birth weight.

Results : 333 articles were identified initially after combining all the key words, with only 133 eligible articles published from 2008 to 2019. After review of the available 50 full text articles, duplicates were removed and 15 studies fully met the inclusion criteria. 13 articles supported the association between maternal periodontitis and preterm and/ or low birth weight while 2 found no evidence to support the association. Although we did not appraise methodological quality or risk of bias of the selected studies, as per the guidelines for scoping reviews, good quality and up to date studies were selected. However, there were some inconsistencies in the findings due to differed case definitions, study settings and sample.

Conclusion : The results of this scoping review are consistent with a previous review of case-control studies only, thereby contributing to an increasing body of evidence to support the hypothesis that periodontal disease may be a risk factor for preterm delivery and low birth weight. More rigorous studies with larger prospective cohorts are needed to provide more conclusive frameworks for testing the suspected clinical association between maternal periodontitis and perinatal outcomes.

Background

Periodontitis is a highly prevalent inflammatory and infectious disease of tooth-supporting tissues leading to oral disability ¹. Periodontal diseases are commonly caused by gram-negative anaerobes that colonize the sub gingival area. Periodontal diseases, are reported to be the most common disease of man kind whereby severe periodontitis is the 6th most prevalent disease worldwide ^{2, 3}. The global burden of periodontitis increased by 57.3% from 1990–2010 ³. Periodontitis, as a chronic non-communicable condition, shares risk factors with the major non-communicable diseases (NCD's) that cause around two-thirds of deaths worldwide, such as heart disease, diabetes, cancer and chronic respiratory disease. A study done in Europe about periodontitis found prevalence rates varied greatly across the continent; 13% in Norway, 12% in the UK, 82% in Sweden, 25% in Switzerland and 80% in France ^{4 5}.

In the United States, the National Health and Nutrition Survey (NHNS) conducted in 2009–2010 estimated prevalence rates in the U.S. population to be as high as 50%⁶ while in Latin America, the prevalence of periodontitis was estimated to range between 40–80%⁷. In India, Shewale and colleagues reported the prevalence rate of periodontitis to be 85% of the general population and recommended the government as well as the dental council to develop and promote interventions in order to improve oral health and thus the quality of life⁹. In addition Bansal and colleagues in their study also found that 96.3% of the population in India had periodontal diseases¹¹.

Houshmand and colleagues reported that periodontitis is very high in many African countries¹². In Nigeria, Akpata reported a high proportion of deep pockets that varies between 5% and 80%¹³. In East Africa, high prevalence of periodontitis was also reported in Kenya, Uganda, Tanzania and Rwanda^{14, 15,16}.

Huck and colleagues have suggested that periodontitis might be linked to increased risk of preterm birth, but the evidence to support this association remains uncertain¹⁷. According to this hypothesis, periodontal infections can serve as a reservoir of inflammatory mediators, and thus may be a threat to the fetal-placental unit and therefore are associated with adverse pregnancy outcomes like preterm birth and low birth weight babies < sup > 18</sup>(18),(19),(20). These inflamed periodontal tissues produce pro-inflammatory cytokines and host the bacteria that can cause inflammation once they get into the blood stream, where they are reported to possibly affect the fetus and result in low birth weight babies. This connection is believed to originate with the deleterious effects of endotoxins released from the Gram-negative bacteria responsible for periodontitis. The potential role of periodontitis as a risk factor for low birth weight (LBW) requires further studies and also suggest a need for further preventive measures for pregnant women and better collaboration between the obstetrical and dental professions¹⁹. Because of the uncertainty and in the literature about the role of periodontitis in preterm low birth weight, there is a need to synthesize the evidence on the impact of periodontitis on preterm low birth weight in order to improve public awareness and to inform policies for oral health during pregnancy. Therefore, the objective of this scoping review is to assess the published evidence testing the association between maternal periodontitis and preterm birth and low birth weight in infants.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extended for Scoping Reviews (PRISMA-ScR) guided this review. The protocol was not registered in any database. Articles were included if they, investigated periodontal disease in pregnancy in relation to gestational period and infant weight, were interested in Human participants and published between the period of 2008–2019, were written in English using either case-control, cross-sectional or randomized controlled trials designs. Papers were excluded if they: did not fit the inclusion framework of the study not primary research reports (e.g. magazine articles, commentaries, letters, etc.).

Electronic databases were used to search for relevant articles. The published literature between January 2008 and December 2019 was searched using the Hinari, PubMed and Google Scholar databases. The search strategies were developed by two authors (P.U & A.N) and refined through the discussion among the rest of the authors. The retrieved articles were exported into Mendeley where the duplicates were removed. Two reviewers (P.U & A.N) screened the titles and abstract independent from each other and disagreement was solved by discussion between them. The same process was used to screen the references. A thorough reading of the full text papers was performed by both reviewers for the papers selected from the initial title review.

Key search terms used were related to periodontal disease, periodontitis, preterm birth, low birth weight, pregnancy and risk factors were used in PubMed using the Medical Subject Heading. For example, in Pubmed, the search of literature was performed using the key terms in the domain of (1) periodontal disease, preterm birth, (2) preterm birth, (3) low birth weight, (4) pregnancy, (5), periodontitis, risk as well as their combination with the limit to English language from 2008 to 2019. The key terms used in Pubmed and other data bases are available in the appendix.

The reviewers used a consensus agreement approach to validate the data extraction form for consistency of the results from title screening and abstract review.

The data that were abstracted include the authors, years of publication, country, study design, population type and sample size and the definition of periodontal disease used in the study. We also reported the main outcome variables and summary of the final conclusion.

Results

The search from the different databases retrieved 320 articles from the initial search as seen in Table 1. After the initial retrieval, these articles were screened based on the titles, years of publication and types of studies. An additional 13 articles were located from the scan of the initial articles. After the screening and combining the key the words, 333 articles remained. From the 333 articles, 200 ineligible and duplicates were removed leaving 133 articles that were published in the last 10 years with human subjects. A total of 93 articles did not meet the study inclusion criteria thus we fully retrieved full text for 40 articles. In this last step a further, 25 articles were removed for a variety of ineligibility reasons, leaving 15 articles published in English from the year 2008 to 2019 (that were selected as shown in Fig. 1).

Table 1
Characteristics of the selected studies.

References Country	Type of study Sample size	Periodontitis definitions	Outcome variables	Conclusions
MUWAZI et al. 2014 Uganda	Cross sectional N = 400	Bleeding on probing, probing pocket depth, calculus with plaque deposits and gingival recession	Birth weight, Gestational age	Bivariate analysis showed a significant association between gingival recession and low birth weight $p < 0.005$
Wang 2012 Taiwan	Randomised controlled trial N = 211 HG = 82 GG = 67 PG = 62	Gingival bleeding > 5%, CAL > 6, PD of 5 mm	Gestational age, birth weight and total maternal weight gain during pregnancy	There is an association between Periodontal diseases and low birth weight but no association b/n PD and PTB $p = 0.030$
Davenport 2012 London, UK	Case control 236 cases, 507 controls	CPITN = 4 mm	Birth weight, Premature deliveries	There is no association between periodontal diseases and PTLBW
Grandi 2010 Argentina	Case control 53 cases 79 controls	Bleeding index of 0–3, CAL > 1, PPD > 30% of involved sites	Preterm birth	Bleeding index and periodontal pockets depths were associated with preterm birth ($p = 0.026, 0.043$)
Cruza et al. 2013 Brazil	Case control 102 cases 200 controls	CAL 4 mm at least 4 teeth	Birth weight	Periodontal disease is a possible risk factor for low birth weight
Satheesh 2011 India	Case Control 52 cases 52 controls	PD \geq 4 mm, CAL \geq 3 mm at the same site in at least 4 teeth	Birth weight, Preterm birth	A noticeable relationship between periodontal diseases and gestational age ($p < 0.005$)

References Country	Type of study Sample size	Periodontitis definitions	Outcome variables	Conclusions
Haerian et al 2013 IRAN	Case control n = 88 44 cases 44 controls	CPITN grade III and IV	Birth weight	The maternal periodontal diseases can be a potential independent risk factor for LBW (p = 0.006)
Vettore et al 2008 Brazil	Case control N = 116		Birth weight	Periodontal diseases were associated with low birth weight
Marakoglu I. et al 2008 Turkey	Case control n = 48 20 cases 28 controls	3 or more sites with 4 mm or more pocket depth, bleeding on probing, alveolar bone loss	Preterm birth, low birth weight	Poor periodontal health status of the mother may be a potential risk factor for preterm low birth weight
Karimi et al 2016 Iran	Case control N = 264 132 cases 132 controls	CPITN	Preterm, low birth weight	Women with periodontal diseases delivered 10 times low birth weight infants and 8 times premature infants that women with no periodontal diseases
Sindhu 2009 USA	Prospective cohort N = 786	Not mentioned	Birth weight, preterm birth	Despite the literature suggesting the association, this cohort study failed to demonstrate the association.
Lohana et al 2016 India	Prospective cohort N = 300	Slight perio CAL = 1–2 mm Moderate perio CAL = 3–4 mm Severe perio CAL ≥ 5 mm	Gestational age, birth weight, BMI	Periodontal diseases is a potential risk factor for preterm low birth weight babies. (p < 0.005)
Kukkamalla et al 2014 India	Case control N = 200 100 cases 100 controls	Not mentioned	Preterm delivery	There was significant correlation of poor hygiene, gingival inflammation, probing depth to preterm delivery and low birth weight.

References Country	Type of study Sample size	Periodontitis definitions	Outcome variables	Conclusions
Khadem et al 2012 Iran	Case control N = 70 35 cases 35 controls	CAL > 3 mm, PPD > 3 mm	Preterm birth, low birth weight	Gum diseases can be a risk factor for preterm delivery. (p = 0.007)
Rakot et al 2010 Madagascar	Prospective cohort N = 204		Preterm birth, low birth weight	There was a strong association among periodontitis, preterm birth and low birth

Among the selected and included articles, there were 10 case control studies, 3 were prospective cohort studies, 1 cross-sectional study and 1 randomized controlled trial. Table 1 shows the characteristics of selected studies.

The results for all the studies considered the periodontal examination was based on the bleeding on probing, probing depth and clinical attachment loss although the exact definitions used varied according to the different studies. The level of evidence was good considering studies with different study designs, samples and methodologies.

Discussion

Periodontitis have been reported to be associated with preterm birth and/or low birth weight worldwide²⁰. However, there is uncertainty in the literature regarding the association between periodontitis and preterm low birth weight. This literature review focused on the results of 15 different studies retrieved from the literature that were conducted to test this association. One key challenge in reviewing the literature was caused by inconsistencies in the definitions of preterm birth, low birth weight and periodontitis used in the studies. Different authors used different ways of defining the key terms under study. Almost all the authors considered the bleeding on probing, pocket depth, calculus and clinical attachment loss (CAL) but the measurements for these parameters for defining periodontal disease varied depending on the authors. For example, some authors considered bleeding on probing, pocket depth and CAL, while others considered bleeding on probing, pocket depth, calculus and CAL and others only considered only pocket depth, and CAL. The variability in these case definitions likely contributed to the heterogeneity of the study results and thus contributes to the overall uncertainty of the validity of the association. There is a need to have a calibrated definition of periodontal disease so that the researchers can have the same understanding of what is being studied. Despite the variability in the case definitions, 13 out of 15 included studies reported an association between periodontal disease and preterm low birth weight with the other 2 studies not finding an association. The variability in the results could also be impacted by differences in the study settings, the sample size, the duration of the study and possible confounding

factors. The studies done in urban settings differed to studies done in rural settings because in urban settings, people may tend to have more advanced knowledge on oral health and better socio economic status both of which are known to have a positive influence on periodontal disease. For example the prospective study in this review done by Sindhu and colleagues, was conducted in an urban setting and this may have influenced the results of no association between periodontal disease and preterm low birth weight because the prevalence of periodontal disease tends to be lower and this may have reduced the study's statistical power²¹. This study by Sindhu was also testing for improvements in perinatal outcomes following periodontal treatment during pregnancy but it failed to show any association with this outcome either. This lack of an association was in agreement with Bansal and colleagues who stated that providing periodontal treatment during pregnancy may be too late to reduce the local and systemic inflammations and may be ineffective in preventing the preterm birth²². The other negative study findings from the case control study in Uganda conducted by Muwazi and colleagues, was possibly limited by the use of only one group of women for a short period of time²³. The other 13 studies retrieved did find an association between periodontal disease and preterm birth and/or low birth weight. Out of the 13 studies that showed positive association, some found an association between periodontal disease and low birth weight only (n = 5, some reported an association between periodontal disease and preterm birth (n = 3), and others reported association between periodontal disease and preterm low birth weight (n = 5).

Kastroit and colleagues reported that women with periodontal disease were 3.2 times more at risk for delivering a low birth weight baby and 3.4 times more likely to deliver premature babies than women without periodontal disease (OR = 3.2, 95% CI 1.5–6.8) and (OR = 3.4, 95% CI 1.6–7.3) respectively²⁴. Also the findings from Karimi and co-authors reported that women with periodontal disease in their study delivered 10 times more likely to deliver low birth weight infants and 8 times more likely to deliver premature infants than women without periodontal disease²⁵. The findings of this review are consistent with a systematic review of case-control studies done by Teshome & Yitayeh, which reported that periodontal disease may be a risk factor for preterm birth, low birth weight or preterm low birth weight and the odds ratios ranged from 2–4²⁶. It has been hypothesized that the inflammatory cytokines such as tumor necrosis factor- alpha (TNF- α) and interleukin-6 (IL-6) which can reach high concentrations in periodontitis cases, stimulate increased prostaglandin production from the amnion and decidua, leading to the onset of preterm labor. This is evidenced by the presence of increased cytokines and prostaglandin levels in preterm birth patients with no other infections like genitourinary tract infections. This supports the idea that preterm low birth weight are results of infections of unknown origin and possibly periodontitis^{27, 28, 29}.

While most studies conducted support this association, as pointed out in this review there are some conflicting findings reported as well. These inconsistencies could arise for a number of reasons, including variations in study settings and case definitions as highlighted earlier in this review.

Table 2 shows periodontal case definitions for some studies in this review.

Table 2
shows case definitions in the selected studies

Author	PD CASE DEFINITION	Results
MUWAZI et al. 2014	0. No periodontal disease 1. Bleeding on probing 2. Calculus with plaque seen or felt by probing 3. Pathological pocket 4– 5 mm 4. Pathological pocket 6 mm or more 5. Gingival recession	Approximately 26% and 29% of the post-partum mothers had gingival bleeding and periodontal pockets of 4 mm or above. Significant association between gingival recession and low birth weight ($p < 0.005$)
Wang 2012	Gingival bleeding > 5% Clinical attachment loss > 6 mm Pocket depth = 5 mm	The periodontal group women had a higher frequency of preterm low birth weight (14.5%). Significant association between periodontal group and low birth weight ($p =$ 0.030)
Grandi 2010	BOP 0–3 mm = Normal PD < 3 mm and < 30% of sites involved = localized PD > 3 mm and > 30% of sites involved = generalized CAL < 3 mm and < 30% of sites involved = localized CAL > 3 mm and > 30% of sites involved = generalized	The Preterm cases showed a higher proportion of bleeding that term cases 86.7% versus 68% and a greater maximum pocket depth on probing 3.9 vs 3.2 mm ($p = 0.043, 0.026$)

Author	PD CASE DEFINITION	Results
Haerian et al 2013	<p>Grade 0: No sign of pockets, calculus and bleeding on probing (gingival health).</p> <p>Grade 1: No pockets, calculus or overhangs but there is bleeding on gentle probing (mild gingivitis)</p> <p>Grade 2: No pockets exceeding 3 mm but there is presence of plaque retaining factors (established gingivitis)</p> <p>Grade 3: 4–5 mm deep pocket (mild periodontitis)</p> <p>Grade 4: pocket depth < 6 mm (severe periodontitis)</p>	Percentage of sextants diagnosed with LBW infants (case group) was 1.6 times more than control group. Mothers with low birth weight infants had less health gingiva and more deep pockets (p = 0.042, 0.006,) Mann-Whitney test
Satheesh 2011	PD > 4 mm and CAL > 3 mm at the same site in at least 4 teeth	A noticeable relationship between periodontal health and duration of pregnancy (p < 0.005)
Lohana et al 2016	<p>CAL 1-2mm: Slight periodontitis</p> <p>CAL 3–4 mm: Moderate periodontitis</p> <p>CAL > 5mm: Severe periodontitis</p>	As the level of periodontal disease severity increases, the proportion of preterm delivery also increases (p < 0.005)
Khadem et al 2012	<p>Extent index: CAL > 1</p> <p>Severity index CAL between sites</p> <p>Probing depth > 3 mm</p>	Gum disease can be a risk factor for preterm delivery (p = 0.007)

Data Quality And Limitations

While there are inconsistencies in this review regarding the association of periodontal disease and preterm low birth weight, there are different reasons among the included studies that may contribute to the uncertainty in the findings. The definitions of preterm birth and low birth weight, are well defined but no consensus has yet been achieved on the definition of periodontitis in periodontal research. A consensus on a definition is important to optimize the interpretation, comparison, and validation of clinical data. Also clinical markers of periodontal disease, such as clinical attachment loss, bleeding on

periodontal probing and periodontal pocket depth were defined considering different measurements. Another potential reason for different findings among the included studies is the differences in the study settings. One of the studies that did not find any association between periodontal disease and preterm low birth weight in this review was conducted in urban setting which may have biased the findings. Finally, the study design was also among the factors for inconsistencies as most of the studies were case control studies they are limited in their experimental design because they cannot demonstrate causality.

Conclusions

This review has found that the clear majority of papers examining the association between maternal periodontal disease and preterm low birth weight have concluded that the association is indeed present. Although there is a significant evidence that supports this association, it is important in future research that the authors clearly specify exactly how they are defining their independent and dependent variables so that the inconsistencies observed in case definitions, study designs and findings can be minimised. Also more detailed and rigorous studies are needed with strong, and ideally prospective designs using more calibrated (i.e consistent) definitions of periodontal diseases so that the level of the evidence for this association can be strengthened.

Abbreviations

NCD's

Non-communicable diseases

NHNS

National Health and Nutrition Survey

LBW

low birth weight

PTLBW

Preterm low birth weight

PRISMA-ScR

Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extended for Scoping Reviews

TNF- α

Tumor necrosis factor- alpha

IL-6

Interleukin-6

PD

Pocket depth

CAL

Clinical attachment loss

TSAM

Training Support Access Model

Declarations

Ethics approval and consent to participate: Not applicable to this study

Consent for publication: This manuscript contains no any individual person's data in any form and consent for publication is not applicable for this section.

Availability of data and materials: Data sharing is not applicable to this article as no data sets were generated or analyzed during this study.

Competing interests: All authors declared no competing interests.

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Authors' contributions:

PU: Searched for articles and participation in manuscript preparation.

PU and AN developed search strategies and refined through the discussion among the rest of the authors. CM, SR, MK and HS have made substantial contributions to the design and critical reading of manuscript. All authors read and revised critically and approved the final manuscript

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Authors' contributions

Conflict of interest

All authors declared no conflict of interest and no competing financial interest.

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Figures

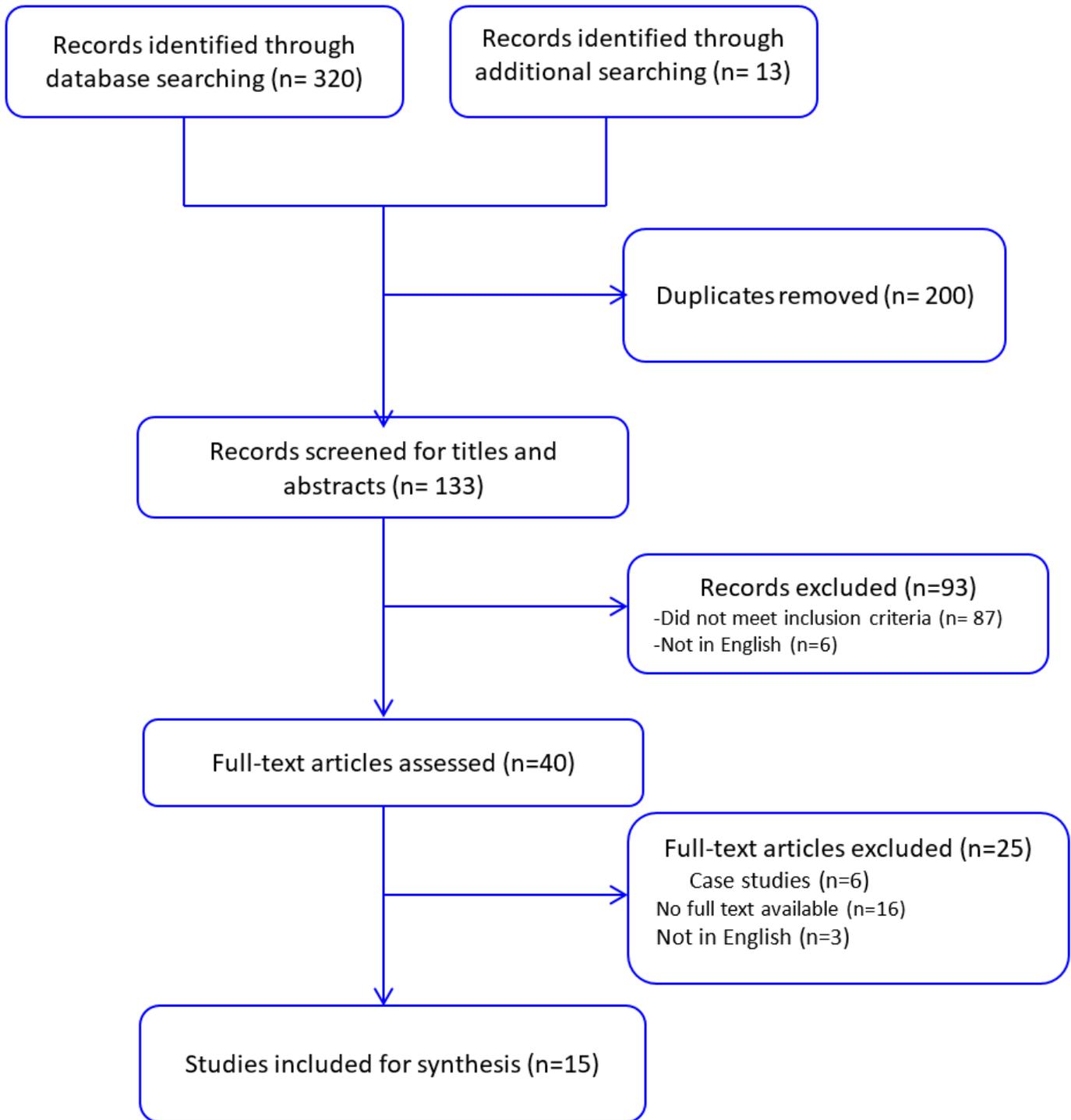


Figure 1

Prisma flow chart for the selected studies