METAANALIZA
położnictwo

Periodontitis and risk of preterm birth and low birthweight – a meta-analysis

Zapalenie przyzębia a ryzyko przedwczesnych porodów i niskiej masy urodzeniowej – metaanaliza

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Abstract

Introduction: *Periodontitis and prematurity are social diseases with common risk factors. In 1996 periodontitis was proven to be a possible significant and independent risk factor of preterm birth of newborns with low body weight. Numerous studies on the influence of periodontitis on the time of birth and/or birth weight of newborns have been conducted throughout the world since, including several ones in Poland, but their results have been inconsistent. Work objective: A meta-analysis of case-control, prospective and cohort studies on the influence of periodontitis on preterm birth and low birth weight.*

Methods: *The international and Polish bibliography bases were searched for essays on the relationship between periodontitis and preterm birth and/or low birth weight published between 1996 and 2010. All essays qualified for the meta-analysis were subjected to qualitative evaluation. The calculation of the overall odds ratio used both, fixed-effects and random-effects models (DerSimonian-Liard method). The heterogeneity of the included studies and effect of publication bias were also subjected to evaluation.*

Results: *The meta-analysis included 15 case-control studies, 1 cross-sectional study, and 6 cohort studies. The essays came from 4 continents: 8 from Europe (including 2 from Poland), 7 from South America, 4 from North America, and 3 from Asia. The total analysis covered 12047 pregnant women. The overall odds ratio of giving premature birth to a child with low weight for mothers with periodontitis in the model of random effects amounted to 2.35 (1.88-2.93, p<0.0001). For low birth weight, the overall OR was 1.5 (95% CI: 1.26-1.79, p=0.001) for premature births – 2.73 (95% CI: 2.06-3.6, p<0.0001). A significant heterogeneity of the studies included in the meta-analysis was observed, and a significant publication bias was also demonstrated.*

Conclusions: *The hypothesis of periodontitis as an independent risk factor of preterm birth and/or low birth weight needs further verification. In order to achieve that, it is necessary to conduct more methodologically well-planned cohort and intervention studies. The need of dental care for pregnant women as an integral component of the prenatal care program remains to be an important issue.*

Key words: **preterm birth** / **low birth weight** / **periodontitis** / **meta-analysis** /

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Streszczenie

Wprowadzenie: *Zapalenie przyzębia i wcześniactwo to choroby społeczne o wspólnych czynnikach ryzyka. W 1996 roku wskazano, że zapalenie przyzębia mogłoby być istotnym i niezależnym czynnikiem ryzyka przedwczesnego porodu noworodka o niskiej masie ciała. Od tego czasu przeprowadzono wiele badań na świecie i kilka w Polsce nad wpływem zapalenia przyzębia na termin porodu i/lub masę urodzeniową noworodka. Ich wyniki były sprzeczne.*

Cel pracy: *Metaanaliza badań kliniczno-kontrolnych, przekrojowych i kohortowych dotyczących wpływu zapalenia przyzębia na przedwczesny poród noworodka o niskiej masie urodzeniowej.*

Metody: *W międzynarodowych i polskiej bazie bibliograficznej poszukiwano prac opublikowanych w latach od 1996 do 2010 na temat związków pomiędzy zapaleniem przyzębia z przedwczesnym porodem i/lub niską masą urodzeniową noworodka. Wszystkie prace zakwalifikowane do metaanalizy były poddane ocenie jakościowej. Dla wyliczenia skumulowanego ilorazu szans zastosowano model efektów stałych i model efektów losowych w metodzie DerSimonian-Liard. Oceniano także jednorodność włączonych badań i efekt obciążenia publikacyjnego.*

Wyniki: *W metaanalizie uwzględniono 15 badań kliniczno-kontrolnych, 1 przekrojową oraz 6 kohortowych. Prace pochodziły z 4 kontynentów: 8 z Europy (w tym dwie polskie), 7 z Ameryki Południowej, 4 z Ameryki Północnej i 3 z Azji. Analizie łącznej poddano 12047 kobiet w ciąży. Skumulowany iloraz szans przedwczesnego urodzenia dziecka o niskiej masie dla matek z zapaleniem przyzębia w modelu efektów losowych wynosił 2,35 (1,88-2,93, p<0,0001). Tylko dla niskiej masy urodzeniowej skumulowany OD wynosił 1,5 (95% CI: 1,26-1,79, p=0,001) a dla wcześniactwa 2,73 (95% CI: 2,06-3,6, p<0,0001). Stwierdzono istotną niejednorodność badań włączonych do metaanalizy. Wykazano także istotne obciążenie publikacyjne.*

Wnioski: *Hipoteza o zapaleniu przyzębia jako niezależnym czynniku ryzyka przedwczesnego zakończenia ciąży i/lub niskiej masy urodzeniowej noworodka musi w dalszym ciągu być weryfikowana. W celu weryfikacji tej hipotezy konieczne jest dalsze prowadzenie dobrze zaplanowanych metodologicznie badań kohortowych i interwencyjnych. Ciągle aktualna pozostaje konieczność prowadzenia opieki stomatologicznej nad kobietą w ciąży jako integralnej składowej programu opieki prenatalnej.*

Słowa kluczowe: **poród przedwczesny** / **niska masa urodzeniowa** / **zapalenie przyzębia** / / **metaanaliza** /

Introduction

Preterm birth (PB) and low birth weight (LBW), defined as birth before 37 weeks gestation to a newborn with body mass below 2500 g, continues to be a significant cause of perinatal mortality and several well-known neonatal diseases. In 2005, 12.9 million births, or 9.6% of all births worldwide, were preterm [1].

The highest rates of preterm birth were noted in Africa and North America (11.9% and 10.6% of all births, respectively), and the lowest were reported in Oceania (6.4%) and Europe (6.2%) [1]. The highest percentage of low birth weight is present in the developing countries, where it reaches two digital numbers. It is higher in Poland (7%) than in most European countries (eg. Iceland - 3.1%, Finland - 4.1%, Sweden - 4.5%, Ireland - 4,9%, Netherlands - 5.4%, Denmark - 5.5%, Italy and France - 6.5%, Spain and Germany - 6.8%) [2, 3].

The recognized preterm low birth weight (PLBW) risk factors include the following [4]: low social and economic status of the mother, maternal age (below 18 and above 35 years of age), previously recorded premature birth, low body mass before the pregnancy, one or more self-induced miscarriages during the second trimester in the case study, diabetes, epilepsy, hypertension, kidney diseases, cardiac defects, sexually transmitted diseases, nicotine addiction, alcoholism, drug addiction, inadequate level of prenatal care. Special attention should be paid to subclinical and clinical bacterial infections (most often of the genitourinary tract), which also influence premature destruction of the placenta.

In 1996 in the USA, Offenbacher et al., [5] were the first in representative case-control studies to point to periodontitis as a significant and independent PLBW risk factor.

Periodontitis is a social disease caused by imbalance between the Gram-negative periodontal pathogens and the defensive mechanisms of the host. Its current incidence in Poland is assessed at 18% in the age group of 35-44 years. In the case of generalized forms of such diseases, the surface of inflammatory alterations reaches as much as 70 cm^2, which is beneficial to the penetration of endotoxins and proinflammatory mediators to the blood circulation. The common PLBW and periodontitis risk factors include the following: age above 35, diabetes, use of tobacco, stress, and low socioeconomic status.

After 1996, there were many non-experimental studies (case-control, prospective and cohort) conducted all over the world on the connection between periodontitis in pregnant women and various adverse perinatal outcomes. Their results were inconsistent, and in most cases, even if the dependency was characteristic, it was significantly lower than that established by Offenbacher's initial studies.

Since periodontal treatment would act as an element of prematurity prevention, the following step, according to the recommendations of evidence-based medicine (EBM), should be a systematic review of the literature on the subject, and application of the meta-analysis to assess the average influence estimator.

Methods

A search for publications in Polish and international medical literature databases was conducted in order to determine the relation between periodontitis and premature low birth weight. Between 1996 and 2010, the Polish Medical Bibliography and the MEDLINE and PUBMED databases were searched for literature and the key words were "*periodontitis*" and "*preterm low birth weight*" and "*premature pregnancy*" and "*low birth weight*". The only essays taken into account were those published in reviewed medical periodicals in English, German and Polish.

The first selection provided 122 essays. The next step was to discard synoptic essays, describing the relationship between periodontitis and premature birth and/or preterm low birth weight or other systemic diseases.

The next step was to apply the following inclusive criteria:

1. non-experimental, case-control, prospective or cohort studies,
2. exposition defined as periodontitis in the mother,
3. cases defined as PLBW or PB (preterm birth – birth before 37 weeks gestation) or LBW (low birth weight – birth weight below 2500g),
4. studies conducted in people; only case parameters were used in periodontium studies (studies establishing immunologic parameters in the gingival fluid and blood serum were not considered),
5. only one (the earliest) study conducted by the same group of authors was considered.

The publications selected in that way served as the source of the following information: demographic data, study inclusion and exclusion criteria, pregnancy age determination method, disturbing variables considered in the studies, dependency evaluation measures.

The articles were read and quality-scored by two independent persons. All essays qualified for the meta-analysis were subjected to qualitative evaluation which used modified criteria according to Margetts and al. [6] (Table I).

The publications qualified for the meta-analysis in order to determine the relationship between the examined pathologies provided the pooled odds ratio (OR) with a 95% – confidence interval (CI) by using the inverse variance method. Since the PLBW risk in the general population is low (does not exceed 20%), the relative risk (RR) was established as the admissible approximation of the OR values. The odds ratios were transformed into their natural logarithms in order to obtain symmetric confidence distributions. The calculation of the overall odds ratio used both fixed-effects and random-effects models in the DerSimonian-Liard method.

The heterogeneity of the studies included in the meta-analysis was examined with the I^2 and Q-Cochran test. The evaluation of the presence of publication bias utilized the correlation test tau-b (with constant correction) and the Egger test. The threshold of significance for all used statistical tests was determined as $p<0.05$.

Results

60 original publications remained out of the 122 essays from the first selection after excluding experimental, casuistic, abstracts and review works. After applying these inclusion criteria, 22 publications in total were qualified for the meta-analysis.

Table I. Criteria of the qualitative evaluation of papers included in the meta-analysis.

Evaluation criteria	% weight in qualitative evaluation
All papers	79% including:
Clinical evaluation of the periodontium (peculiar?, proper? several methods?)	9%
Pregnancy age description (defined, correct?)	9%
General description of the study methodology (clear?, correct, zero hypothesis?)	4,5%
Inclusion/exclusion criteria (defined, justified?)	4,5%
Number of cases: quantitative study (from 1 to over 1000)	16%
Number of cases: justification (prior calculation of the number)	3%
Date of study?	2%
Study duration?	2%
Calibration of the studies (definition, value?)	5%
Disrupting variables (quality?, definition?, correction?)	14%
Presentation of uncorrected results (yes/no)	2%
Presentation of average values of clinical parameters of the periodontium?	2%
Listing OR/RR in relation to the level of clinical parameters?	2%
Statistical analysis (description?, proper?)	2%
Other results (compliance with scientific findings)	2%
Case-control studies	21% including:
Number of control cases per 1 in the studied group (>or<1)	3%
Answer factor (defined?, value?)	7%
Identification of the studied group with no knowledge on the condition of the periodontium	3%
Blinding of the periodontium condition in the case-control status	3%
Intergroup compliance of demographic and medical description	3%
Intergroup methods of data collection compliance	2%
Cross-sectional or cohort studies	21% including:
Answer factor (defined?, value?)	6%
Follow-up factor (defined?, value?)	7%
Study time (pregnancy age at initiation: defined?, proper?)	8%

Table II. Description of studies included in the meta-analysis.

Author and year	Continent Country	Prematurity criteria	Studied indices	Disrupting variables Exclusion criteria	Quality factor
Case-control studies					
Offenbacher et al. (5) 1996	North America, USA	PLBW	BOP, PD, CAL	1-3, 6,7, 9,10-14 2,4,6	51%
Lopez et al. (7) 2002	South America, Chile	PLBW	PI, BOP, PD, CAL	1-4,6-15 2,4,6	49%
Konopka et al. (8), 2003	Europe, Poland	PLBW	BOP, PD	1,2,4,6,9,14 3,7,15	30%
Goepfert et al. (9), 2004	North America, USA	PB	BOP, CAL	1,5,6,9,11,14 N/A	54%
Betleja (10), 2004	Europe, Poland	PLBW	PI, BOP, PD, CAL	1-4, 6,9,12,14 2,3,6	44%
Jarjoura et al. (11), 2005	North America, USA	LBW	PI, BOP, PD, CAL	1,5-11,14 2,3,15	67%
Noack et al. (12), 2005	Europe, Germany	PLBW	PI, BOP, PD, CAL	1,2,5,9-14 1-4, 6,8,15	66%
Moliterno et al. (13), 2005	South America, Brazil	PB	PD, CAL	2,5,6,9-11 1,2,4	44%
Radnai et al. (14), 2006	Europe, Hungary	PLBW	PI, BOP, PD	1,5,9,10,12,14 2	42%
Bośnjak et al. (15), 2006	Europe, Croatia	PB	PD, CAL	1,2,6,7-10,12,14 3,15	38%
Siqueira et al. (16), 2007	South America, Brazil	LBW	BOP, PD, CAL	1-4,6,9,10,12,14 N/A	30%
Bassani et al. (17), 2007	South America, Brazil	LBW	PD, CAL	1-3, 5-7,9-12,14 3	58%
Gomes-Filho et al. (18), 2007	South America, Brazil	PLBW	BOP, PD, CAL	1,2,5,6,9,10,12,14 2,4	58%
Marakoglu et al. (19), 2008	Asia, Turkey	PLBW	BOP, PD	1-3, 5,6,9,10,12,14 4,6	29%
Khader et al. (20), 2009	Asia, Jordan	PLBW	PI, PD, CAL	1,2,5-7, 14 3,4,9,10	35%
Cross-sectional study					
Lunardelli et al. (21), 2005	South America, Brazil	PLBW	BOP, PD	1,5-7, 9-14 1-3, 8	80%
Cohort studies					
Jeffcoat et al. (22), 2001	North America, USA	PB	PD, CAL	1,4,9,11,14 2	31%
Moore et al. (23), 2004	Europe, Great Britain	LBW	PI, BOP, PD, CAL	1-7, 9-11,14,15 2	82%
Rajapakse et al. (24), 2004	Sri Lanka Asia	PB	PI, BOP, PD,	1,2,5,11,12,14,15 1,2,9,10,	52%
Dortbudak et al. (25), 2004	Europe, Austria	PLBW	BOP, PD	1,2,4,6,9,10 N/A	32%
Agueda et al. (26), 2008	Europe, Spain	PB	PI, BOP, PD, CAL	1-6,9-12,14,15 2,4,8,10	68%
Arteaga-Guerra et al. (27), 2010	South America, Columbia	PB	PI, BOP, PD, CAL	1 , 2 , 1 3 , 1 4 1,2,4,9,10,12	37%

1 – Age; 2 – Maternal general diseases (hypertension, diabetes, asthma, cardiovascular disorders); 3 – uterus/placenta/foetus irregularities; 4 – treatment during pregnancy (antibiotics, corticoids); 5 - socioeconomic status; 6 – genitourinary tract infections; 7 – other infections; 8 – number of teeth in the oral cavity; 9 – use of tobacco (before and/or during pregnancy), 10 – alcohol, medicine pre- and during pregnancy; 11 – ethnicity; 12 – prenatal care state; 13 – stress; 14 – obstetric history; 15 – type of delivery

PI – plaque index
BOP – bleeding on probing
PD – pocket depth
CAL – clinical attachment loss

The descriptions of the included studies are presented in table II. The analysis covered 15 case-control studies, 1 cross-sectional study, and 6 cohort studies conducted between 1996 and December 2010. The works came from 4 continents: 8 from Europe (including 2 from Poland), 7 from South America, 4 from North America, and 3 from Asia. The total analysis covered 12047 females, including 1898 cases of PLBW or one of its components. The combined studies used various prematurity criteria (PLBW in 11 studies, PB in 7 and LBW in 4), as well as various definitions of periodontitis. The studies greatly varied in the qualitative evaluation of the work (from the highest for the Moore et al. study [23] - 82%, to the lowest for the Marakoglu et al. study [19] - 29%). All studies recognized age and smoking as significant disturbing variables or exclusion criteria.

Figure 1 presents a forest plot of the odds ratio (OR) with a 95%-confidence distribution for PLBW in mothers with periodontitis in comparison to mothers with periodontitis giving birth to newborns with proper body weight at term. The overall PLBW odds ratio for mothers with periodontitis in the random effect model was 2.35 (1.88 - 2.93, $p<0.0001$). In 21 studies, the OR was higher than 1, including the level of statistical significance in 16 of them [2, 4-8, 10-13, 15-17, 19, 22, 23). For LBW itself the overall OR was 1.5 (95% CI: 1.26 – 1.79, $p=0.001$), for PB 2.73 (95% CI: 2.06 – 3.6, $p<0.0001$).

Figures 2 and 3 present forest plots of the odds ratio with 95% confidence of distribution separately for low birth weight and preterm birth at mothers with periodontitis, retrospectively.

A significant heterogeneity of the studies included in the meta-analysis was determined (Q Cochran test result = 52.44, $p=0.0002$, and $I^2 = 59.95\%$).

A significant publication bias was also established (tau-b test correlation factor value = 0.48, $p=0.001$, and Egger test: $p=0.002$). This is also confirmed by the funnel plot, where the vertical axis presents the standard error, and the horizontal axis presents the value of the OR natural logarithm. (Figure 4).

This probably results from recognizing only the results of published essays in the meta-analysis, which usually favor characteristic statistical results (the earlier studies especially demonstrated the influence of the first Offenbacher et al., publication on this correlation).

Discussion

To the best of our knowledge, the presented paper is the third meta-analysis of case-control, cross-sectional and cohort studies on the association between periodontitis and preterm birth and/or low birth weight. (Table III). As the first two, the study confirms the significance of this dependency. The current analysis covered the highest number (12471) of pregnant mothers. However, our studies point to the heterogeneity of the analyzed data, and the conduction of significant publication bias. Such factors require careful interpretation of the confirmed dependency, and point to the necessity to critically analyze numerous, especially early, studies on this subject.

The first meta-analysis of Khader and Ta'ani [28] considered only 5 publications (including 3 American). The quality factor of the considered publications varied from 71.2 to 35.44. The authors do not exclude the possibility of publication bias (no adequate tests were conducted) and point to three limitations of the conducted meta-analysis: only studies in English were considered, the quality factor of the study providing 55% of the analyzed cases was the lowest, and the control of disturbing factors was inadequate.

The broad review of the early studies (until March 2005) on the association between periodontitis and adverse perinatal outcomes was performed by Xiong et al. [29]. They did not calculate the overall OR, but they noticed the heterogeneity and publication bias of the previous studies. The reasons for this state were searched for in the following: diversity of accepted definitions of periodontitis, errors in forming the exclusion criteria and failure to recognize several disturbing factors, significant differences among studies conducted in the USA, the developing countries and the European countries (varied social and economic, race, prenatal care level factors, periodontitis incidence) and diversity in definitions of perinatal complications (PB, LBW, PLBW,

Table III. Meta-analyses of the association between periodontitis and preterm birth and/or low birth weight.

Author	Publication years	Number and type of publications	Number of combined cases	Established dependencies for periodontitis (OR)
Khader et Ta'ani [28]	1966-2002	5 studies: 2 case-control and 3 cohort	2369	LBW: 2.3 (1.21-4.38) PB: 4.28 (2.62-6.99) PLBW: 5.28 (2.21-12.62)
Xiong et al. [29]	1966-2005	22 studies: 13 case-control and cross-sectional and 9 cohort	10245	LBW: 6 significant, 1 not PB: 8 significant, 4 not PLBW: 5 significant, 3 not OR cumulated values not calculated
Vergnes J-N, Sixou M. [33]	1966-2005	17 studies: 11 case-control, 2 cross-sectional and 4 cohort	1056/7151	LBW: 4.03 (2.05-7.93) PB: 2.27 (1.06-4.85) PLBW: 2.83 (1.95-4.1)
The current analysis	1996-2010	22 studies: 15 case-control, 1 cross-sectional and 6 cohort	1896/12471	LBW: 1.5 (1.26-1.79) PB: 2.73 (2.06-3.6) PLBW: 2.35 (1.88-2.93)
Fogacci et al. [35]	1996-2010	14 intervention studies	2975	LBW: 1.03 (0.76-1.4) PB: 0.93 (0.65-1.3) PLBW: not available

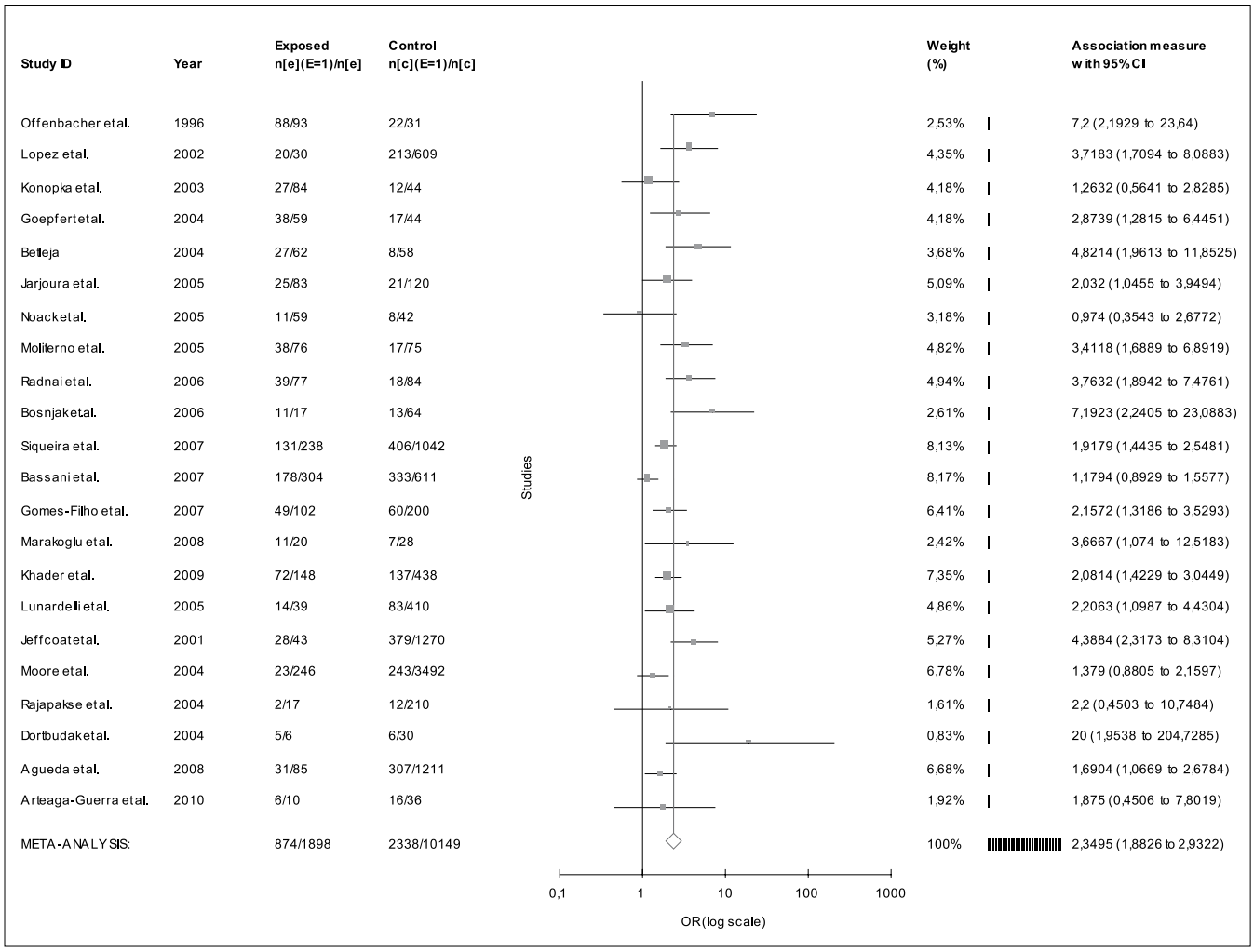

Figure 1. Forest plot of the odds ratios (OR) with a 95% CI for occurrence of PLBW for mothers with periodontitis.

preeclampsia, miscarriage, stillbirth). The early studies had many methodological errors: failure to recognize significant disturbing factors, small group numbers, diversity of periodontium clinical state evaluation protocols, differences in assumed statistical analysis. The more studies qualified for meta-analysis between 1996–2004, the higher the possibility of overestimating the studied dependency. The highest quality factor for studies from that period in the current studies was only 54% [9]. A significant factor may be the diversity in the percentage of prematurity and periodontitis in mothers among individual continents (highest in North America, followed by Asia, South America, and Europe).

A more detailed analysis of the diversity of the definition of periodontitis and pregnancy age is important to interpret earlier studies on the matter. Manau et al. [30] noticed that between 1996-2007, such studies defined periodontitis in 14 ways (the current meta-analysis recognizes 10 of them). Therefore, some variations in the presented OR values should be attributed to the inconsequence in defining the threshold in which the clinical state of periodontium allowed to recognize periodontitis. It has been proven that the acceptance of various definitions of periodontitis produced odds ratio results confirming the influence on prematurity, indicating its insignificant or even protective influence [31]. Presently, the most correct definition of periodontitis is considered to be the Page and Eke definition [32]: a minimum of 2 interproximal sites with clinical attachment level of minimum 4 mm, or a minimum of 2 interproximal sites on different teeth with minimum pocket depth of 5 mm. None of the previous studies on the relationship between periodontitis and perinatal complications accepted such a definition. A gold standard for defining pregnancy age in epidemiological studies is the date of the most recent menstrual period [acc. to 31].

In the absence of that information, the Capurro indicator should be applied. Thus, the least sensitive parameter for diverse definitions of pregnancy age is the low birth weight (LBW).

The current meta-analysis presents an average value of the quality factor for studies relating to LBW as 59.25%, and for PB complication as 54%.

The meta-analysis of Vergnes and Sixou [33], that investigates studies conducted until September 2005, confirms a significant relationship between periodontitis and perinatal complications (LBW, PB, PLBW). (Table III).

The heterogeneity of 17 studies included in the meta-analysis has also been confirmed. The authors described a very significant reverse dependency between the value of individual odds ratios and quality factors of the study, i.e. the higher the methodological quality of the study, the lower the dependency

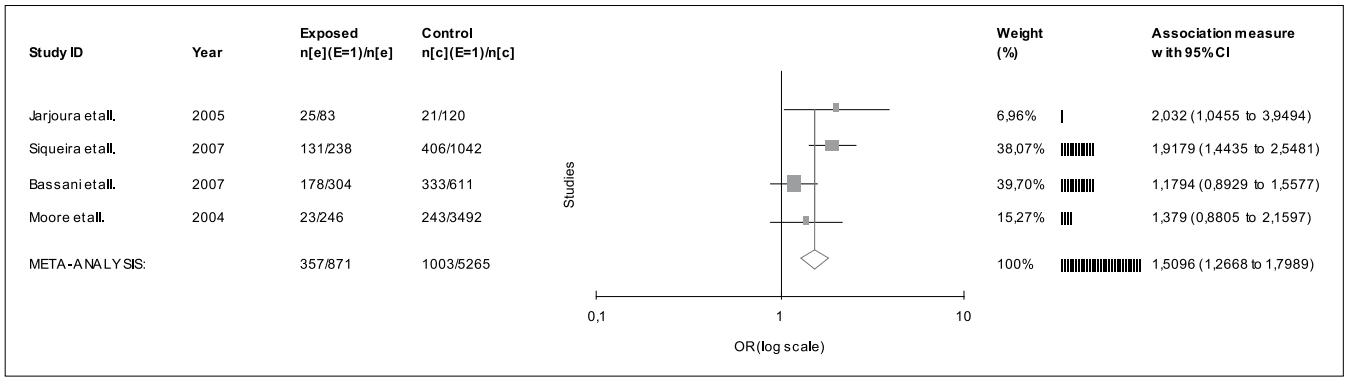

Figure 2. Forest plot of the odds ratios with 95% CI for occurrence of low birth weight for mothers with periodontitis.

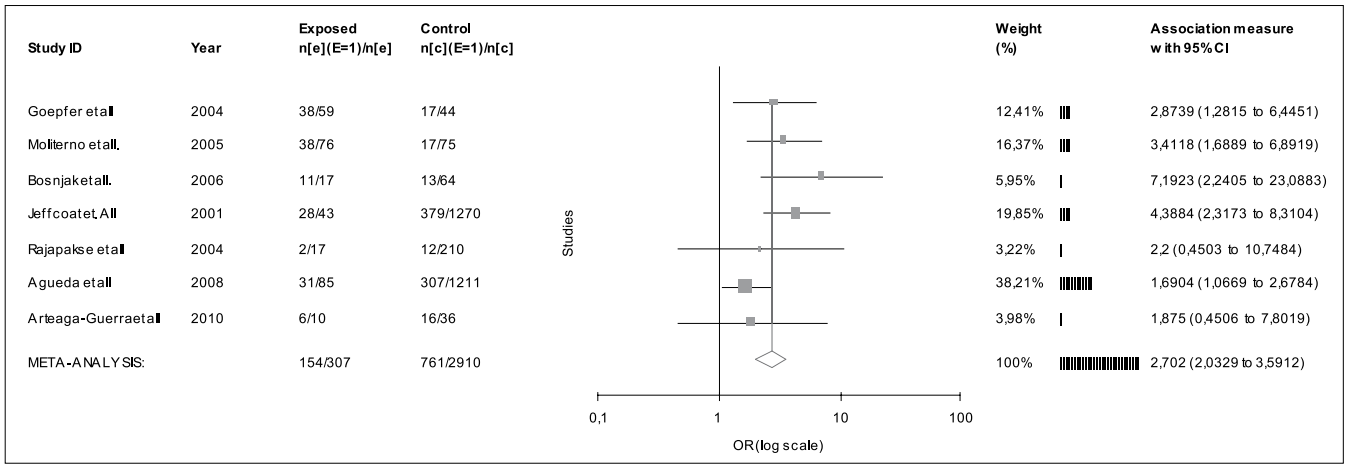

Figure 3. Forest plot of the odds ratios with 95% for occurrence of preterm birth for mothers with periodontitis.

between these pathologies. The earlier studies (1996-2004) had inferior quality and higher dependency factors. The meta-analysis of Vergnes and Sixou [33] presented an average value of the quality factor from 10 studies conducted between 1996 and 2004 as 51.8, in contrast to 59.2 from 7 studies from 2005. The current study presented the average value of the quality factor from 9 studies conducted between 1996 and 2004 as 47.2, and between 2005-2010 as 50.1. The most significant two components deciding on the quality evaluation of the study are the number of groups and consideration of variables disturbing the observation. The most significant disturbing variables which must be considered in such studies include the following: chronic diseases (e.g. diabetes, hypertension, cardiovascular disorders), genitourinary tract infections, antibiotic treatment, as well as prior periodontal treatment. The number of remaining teeth is also important, since in case of residual teeth, periodontitis may curiously produce an improved clinical state of the periodontium. In scope of disturbing variables and criteria for exclusion from studies, the discrepancies among individual observations are very significant. (Table II).

It is a serious cause of the observed heterogeneity of the studies included in the meta-analyses of that issue. Vergnes and Sixou [33] also proved that such factors as the social and economic status and race are very significant for the heterogeneity of such studies. Failure to correct the dependencies with all of these factors leads to statistical overestimations.

The strongest evidence of the relationship between the two pathologies is its confirmation in well-planned intervention studies. On a smaller level, such studies carry a publication bias. In the examined case non-surgical periodontal treatment conducted between 21 and 35 weeks gestation would significantly reduce the percentage of adverse perinatal outcomes. Such influence has been under observation since 2001 [34]. The first meta-analysis [35] summarizing randomized controlled trials on the effect of periodontal therapy of almost 3 thousand mothers on the birth date and body weight of the newborn in 14 intervention studies conducted between 2001 and 2010 has been conducted (table 3) but the significance of such influence has not been confirmed. The OPT (Obstetrics and Periodontal Therapy) study also failed to confirm the influence of aggressive periodontitis in pregnant women on the prematurity and reduced newborn body mass, as well as the relief of such effects in consequence of periodontal treatment [36]. Although recent studies [37] suggest a multifactorial - genetic, social and medical - background of preterm delivery, the periodontal aspects still should not be ignored and taken into consideration in PB and PLBW.

Despite all doubts, there is still not enough evidence to change the guidelines on dental care for pregnant women and make it an integral component of prenatal care. The oral cavity hygiene and non-surgical treatment procedures that should be implemented in such cases are not expensive, and can be performed by every dental surgeon.

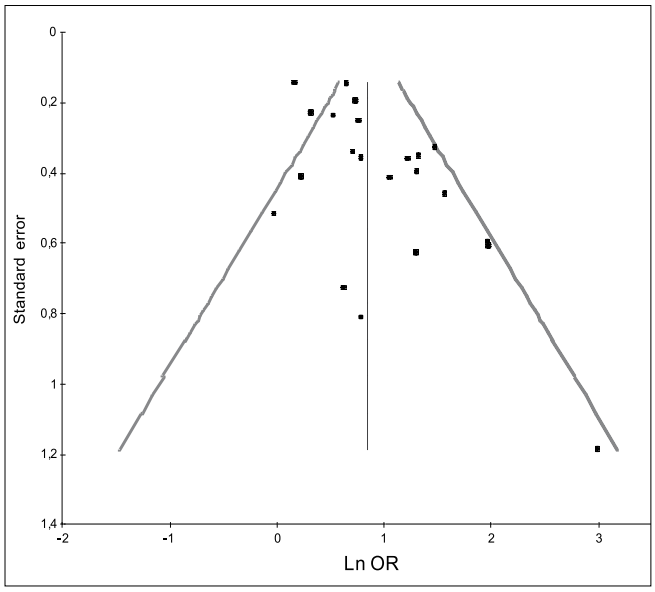

Figure 4. Funnel plot for the evaluation of the publication bias.

Conclusions

1. The hypothesis of periodontitis as an independent risk factor of premature pregnancy termination and/or low body weight of newborns remains to be in need of further verification.
2. In order to verify this hypothesis, it is necessary to conduct more methodologically well-planned (periodontitis and pregnancy age definition, consideration of disturbing factors and adequate exclusion criteria) cohort and intervention studies.
3. There exists a need to conduct good-quality, multi-center Polish cohort and intervention studies on representative material.
4. Dental care for pregnant women as an integral component of the prenatal care program ought to be established.

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