

University of Szeged  
Albert Szent-Györgyi Medical School  
Doctoral School of Clinical Medicine

**The significance of maternal periodontal status  
in prenatal care**

Ph.D. Thesis

Petra Völgyesi M.D.

Supervisor:

Tibor Novák M.D., Ph.D., Med. Habil.

Szeged

2023

## 1. Contents

<b>1. Contents .....</b>	<b>2</b>
<b>2. List of scientific publications related to the subject of this thesis .....</b>	<b>4</b>
<b>3. List of abbreviations .....</b>	<b>5</b>
<b>4. Introduction .....</b>	<b>6</b>
4.1. Periodontal screening during pregnancy .....	6
4.2. The pregnancy-induced hormonal effects on the periodontal status .....	6
4.3. Preterm birth.....	8
4.3.1. The definition of preterm birth .....	8
4.3.2. The importance of preterm birth .....	8
4.3.3. The short and long-term consequences of preterm birth .....	9
4.3.4. The factors leading to predisposition to preterm birth .....	10
4.4. Connection between maternal periodontitis and preterm birth or discrepancies in the scientific literature .....	13
4.5. The role of periodontopathogenic bacteria in the development of periodontal diseases .....	15
4.6. The potential pathomechanism of the connection between periodontal diseases and preterm birth.....	16
4.6.1. Scientific exploration in search of the potential pathomechanism .....	16
4.6.2. Direct and indirect mechanisms.....	17
4.7. Adequate examination practices in relation to periodontitis .....	18
<b>5. Aims.....</b>	<b>18</b>
<b>6. Material and methods.....</b>	<b>19</b>
6.1. Materials and apparatus.....	19
6.2. Method .....	20
6.3. Statistical analysis and graph editing.....	21
<b>7. Results .....</b>	<b>22</b>
7.1. The gestational age at periodontal examination, gestational and maternal age at delivery and birth weight at delivery .....	22
7.2. Comparison of gestational age at periodontal examination in different status groups ..	23
7.3. Correlation between sulcus bleeding index and gestational age at periodontal examination in different status groups.....	24
7.4. Correlation between sulcus bleeding index and gestational age at periodontal examination in the Gingivitis group .....	25
7.5. Correlation between sulcus bleeding index at periodontal examination and gestational age at delivery in all groups .....	27

7.6. Correlation between sulcus bleeding index at periodontal examination and gestational age at delivery in the Gingivitis group .....	28
7.7. Correlation between sulcus bleeding index at periodontal examination and birth weight in different status groups.....	30
7.8. Correlation between sulcus bleeding index and birth weight in the Periodontitis group .....	31
<b>8. Discussion.....</b>	<b>32</b>
8.1. Relationship between oral hygiene during pregnancy and obstetrical outcomes .....	32
8.2. Reasons for the belated detection of periodontal diseases amongst pregnant women ..	33
8.3. Research data.....	34
8.4. The relevance of adequate oral hygiene.....	35
<b>9. Conclusions .....</b>	<b>37</b>
<b>10. Acknowledgements .....</b>	<b>38</b>
<b>11. References .....</b>	<b>39</b>
<b>12. Scientific publications related to the subject of the thesis and appendices.....</b>	<b>43</b>

## 2. List of scientific publications related to the subject of this thesis

1. **Petra Völgyesi**, Márta Radnai, Gábor Németh, Krisztina Boda, Elena Bernad, Tibor Novák. *Maternal Periodontal Status as a Factor Influencing Obstetrical Outcomes*. Medicina 2023, Volume 59, Issue 3, 621. **IF: 2.948**
2. **Völgyesi Petra**, Radnai Márta, Németh Gábor, Boda Krisztina, Novák Tibor. *A fogászati szűrővizsgálatok jelentősége a terhesgondozásban*. Magyar Nőorvosok Lapja 2023. **Under publishing**

### 3. List of abbreviations

ANOVA	Analysis of Variance
BOP	bleeding on probing
BW	birth weight
CRP	C-reactive protein
ELBW	extremely low birth weight
G	Gingivitis
GA	gestational age
GCF	gingival crevicular fluid
H	Healthy
IL	interleukin
LBW	low birth weight
N	number of the patients
P	Periodontitis
PB	preterm birth
PD	probing depth
PGE <sub>2</sub>	prostaglandin E <sub>2</sub>
PIC / NIC	Perinatal / Neonatal Intensive Center
r	correlation coefficient
SBI	sulcus bleeding index
TNF- $\alpha$	tumor necrosis factor alpha
VLBW	very low birth weight
WHO	World Health Organization

## 4. Introduction

### 4.1. Periodontal screening during pregnancy

Even though dental screening during pregnancy is compulsory for pregnant women receiving prenatal care and funded by the healthcare system in Hungary, according to domestic research it is an opportunity rarely used by patients [1]. In our country, participation in the dental screening during the gestational period, funded by the National Health Insurance Fund of Hungary (Hungarian acronym: NEAK) is not a condition for the payment of benefits during and after pregnancy [2].

There may be major differences in the attendance of periodontal screening across various counties and settlements, and it is also impacted by the level of education and social circumstances. According to Hungarian studies, pregnant women are seldom aware of the possibility, but more importantly the significance of periodontal screenings and treatment during pregnancy [1].

In the last years, the connection between periodontal diseases during pregnancy and obstetrical outcomes has been the subject of many research groups' work. The essence of these studies is often the examination of the periodontal status and the preterm birth (PB) and low birth weight (LBW), including all respective maternal and fetal complications [3].

### 4.2. The pregnancy-induced hormonal effects on the periodontal status

Pregnancy is a unique period in a woman's life when different physiological changes happen in the cardiovascular, respiratory, renal, gastrointestinal, hormonal, neurological and haematological systems. Several factors affect the oral hygiene of a pregnant woman. First, the eating habits change. Certain foods may trigger appetite or disgust. In order to aid the absorption of nutrients, the stomach and the intestines discharge more slowly causing symptoms like digestive difficulties (e.g. nausea, vomiting, heartburn, constipation) [4]. The vomitus increases the acidity in the oral cavity potentially leading to the erosion of the tooth enamel [5]. Around 70-85% of women experience these symptoms which normally cease after the first trimester. However, the symptoms may persist among a small proportion of women (0.3-2%); others may suffer from hyperemesis gravidarum which is the graver case of queasiness and vomiting, leading again to the potential erosion of tooth enamel due to the acidity [5].

Apart from the pH change due to the pregnancy-related vomiting and the resulting xerostomia or the deteriorating oral hygiene caused by the more frequent eating, the pregnancy-related hormonal changes have a substantial impact on the status of the oral mucosa, the periodontium, and the dentition. During gestation, the composition of the saliva, and the normal oral cavity flora change, and the secretion of saliva increases (especially in the first trimester), nevertheless, the saliva's neutralising, antibacterial effect declines. The change in the saliva's composition during gestation and lactation may render the teeth more susceptible to erosion and caries [6]. The amount of dental plaque may also increase during pregnancy, just as the predisposition to gestational gingivitis [7].

As a result of the pregnancy-related hormonal changes (i.e. increase in the progesterone level), the gingival capillary dilatation and permeability in the gingival tissues and the periodontium increase [8], allowing the bacteria and/or their products easier access into the periodontal pocket wall tissues than normal [9]. The gingiva becomes more prone to suffer from oedema or bleeding [10], that can be exacerbated by the inadequate oral hygiene.

During pregnancy the keratinisation of the gingiva declines due to the elevated oestrogen and progesterone levels, which also leads to an increase in the permeability of the mucosa, hence the epithelial barrier resistance deteriorates [11]. Therefore, gingivitis and gingival bleeding can develop more easily with the same number of bacteria during pregnancy. Since the sensitivity of the gingiva hinders adequate cleansing, this raises the risk of caries, as well. The gingival erythema with oedema and bleeding can develop at any stage during the pregnancy, however, gingivitis is the most prevalent at the second and third trimester.

Gingivitis is a fairly mild, easily treatable, reversible condition caused by the accumulation of bacterial plaque on the teeth and in the sulcus around the teeth. This is the condition that occurs the most frequently amongst pregnant women (in 65-70% of the cases) [12]. The evolving layer of bacteria irritates the gingiva and causes oedema and gingivitis. It may cause bleeding, experienced most often when brushing or flossing teeth or biting into harder food (e.g. apple). Around the teeth, periodontal pockets develop between the gingiva and the teeth which then would become deeper by the inflammation becoming chronic and the lack of adequate periodontal treatment, eventually destructing the tooth-supporting structures (i.e., the gingiva, periodontal ligament, and/or alveolar bone). This can lead to inflammation, periodontitis. In the case of this process further developing, the recession of the gingiva, the loosening of the teeth, even losing teeth may threaten.

The pregnancy-induced hormonal changes thus may increase the risk of periodontal diseases and exacerbate existing pathological conditions of the periodontium [13, 14].

Immunological changes during pregnancy also affect the oral health. The suppression of certain neutrophil functions may also explain the exacerbation of gingivitis. This is a relevant factor in the development of periodontal disease during pregnancy [15].

Previous studies stated that the inadequate periodontal status, the existence of dental diseases may lead to several negative effects on the obstetrical outcome, concerning the gestational age (GA) at delivery and the birth weight (BW) [3].

### 4.3. Preterm birth

#### 4.3.1. The definition of preterm birth

We identify PB when the delivery happens before completing the 37th gestational week. When the GA is difficult to assert, identifying PB may be based on the BW, i.e. in case it is lower than the threshold of 2500 g. The World Health Organization (WHO) classifies premature babies by their BW: babies under 2500 g are LBW, under 1500 g very low birth weight (VLBW), and under 1000 g extremely low birth weight (ELBW) babies.

Based on the outcome, the pregnancy consists of 5 stages: between the 0 and 24th week it is identified as miscarriage; 24th to 28th week it is extremely preterm, 28th to 32nd week it is very preterm, 32nd to 34th week it is moderate preterm and 34th to 37th week it is late preterm babies being born [16].

#### 4.3.2. The importance of preterm birth

PB is a leading cause of morbidity and mortality among newborn babies and is thus a global health problem [17]. Preterm births are responsible for 75% of the perinatal mortality and over 50% of long-term morbidity [18]. Should a premature baby be born before the 34th gestational week, its chances for a healthy life would be significantly lower. The WHO data informs that approximately 15 million preterm births happen in the world every year [19], which exceeds the ratio of 1 baby out of 10. PB is a major issue even in developed countries, it is estimated that 11% of pregnancies end with PB [20]. Risk factors have been identified that may be connected to PB, e.g. age, smoking, alcohol, infections, etc, in the past years [21].

About 1 million babies lose their lives every year which may be linked to the complications of PB. Across the world, the main reason children under 5 lose their lives is prematurity. Dire inequalities can be detected in the survival rates across the world. In low-income countries,



half of the babies born at the 32 weeks threshold (essentially 2 months early) or before, lose their lives in lack of warmth, breastfeeding support, and basic care for infections and breathing difficulties, even though this basic care is feasible and affordable. The vast majority of these babies survive in well-off countries. In middle-income countries, preterm babies surviving the neonatal period face the difficulties of inadequate use of the available technology [22].

In Hungary, more than three-quarters of the perinatal morbidity and mortality is due to premature birth. The ratio of PB is fairly high in Hungary with a very slow decline over the past decade; it is consistently around 8-9%, hence the lower ratio of 6-7% representative in the other European countries hasn't been reached yet [23]. In Hungary during the early 1990's this ratio exceeded 9%, then in 2017, it decreased to 8.3% [24]. This is a higher record than the average for the European Union which in late years was typically around 6%, reaching 6.1% in 2019 [25].

Premature birth brings a higher mortality risk, too, so the ratio of premature babies can significantly affect the infant mortality frequency. The infant mortality hit a historic minimum in 2017 when it was successfully lowered to under 4‰. During the period between 2007 and 2017, it decreased from 5.9 to 3.6‰, identical to the European indicators. According to the statistical analysis, infant mortality is the only demographic indicator able to have demonstrated such an improvement in Hungary over the past decades [24].

Based on the trends, PB is more closely connected to the survival chances of those premature babies born with very low weight between 1000 and 1500 g. In the year 2017, 1.4% of the babies born alive were born with weight under 1500 g, and 0.6% of them under 1000 g. Premature babies most often weigh between 1500 and 2499 g at birth. There is a considerable change in Hungary in relation to the decline in infant mortality based on BW, especially regarding the survival chances of the very preterm babies. The mortality of the ELBW babies dropped to a quarter over the past 30 years, however, the most significant change occurred with the VLBW babies with the mortality rate reduced to less than 10%. While in 1990 only 19% of the ELBW babies lived to their first birthday, this ratio increased to 79% by 2017 [24].

The indicators of perinatal mortality and infant mortality demonstrate the level of development in both the health culture of the country and the care systems.

#### 4.3.3. The short and long-term consequences of preterm birth

The lower the GA is at the delivery, the higher the risk is for permanent impairment and the development of chronic diseases [26]. The lower the BW, the more difficult the newborn's

adaptation to the extrauterine life is expected to be. Since premature babies are born before time, at various levels of immaturity, permanent impairments with shorter or longer-term consequences are expected for some of them.

Infantile respiratory distress syndrome (IRDS) due to the immature respiratory tracts and all conditions arising from the similarly immature circulation, immune system, and thermoregulation system that burdens the adaptation to life after birth are some of the short-term consequences.

Should the premature baby reach the first birthday, the chances are higher for long-term consequences, such as cardiovascular diseases, neurological damage, visual and hearing impairments (shortsightedness, blindness, deafness), personality disorders and learning difficulties, behavioural issues (hyperactivity), and coordination problems.

Preventive medical interventions are recommended to apply to avoid neurologic, sensory and motor impairments, also malnutrition issues, since PB and LBW may involve the risk of a predisposition to these conditions [27]. Premature babies normally offset their deficit in maturity with those born on time by the age of 3 to 6 years, this, however, most often requires regular development activity and permanent treatment. For this exact reason, PB poses a severe challenge to the individual, the family, and the whole society. The lower threshold of premature birth has recently been modified from 28 to 24 weeks as a result of the increasingly encouraging survival rate, the extension of the viability limits, and the reduction in chronic complications, all due to the sudden development in the regionalised premature baby care (Perinatal / Neonatal Intensive Center, PIC / NIC) in the past 20 years [28].

#### 4.3.4. The factors leading to predisposition to preterm birth

The multiple factors leading to PB render prevention difficult. Demographic factors, environmental and other negative circumstances can be conducive to PB, just as existing illnesses, previous operations, and obstetrical anamnesis.

Considering the demographic overview of mothers, a report found women who were classified as black, African-American and Afro-Caribbean were at higher risk of preterm delivery than white women. When comparing, black women experienced a PB rate of 16-18%, as opposed to white women, for whom a rate of 5-9% of PB was recorded. The rate of very early preterm birth was also the highest for black women, its likelihood being three or four times the rate in any other ethnic group [29].

The incidence of PB and LBW increases with children conceived at a too-low or too-high maternal age. According to the data recorded in Hungary in 1990 and 2016, the occurrence of PB and LBW was at its lowest among mothers aged between 20 and 29 years and its highest at the age over 40 or under 14 years. The risk drastically dropped for women at a later age (over 40) in 2016, likely due to the development of medicine, enlarging the spectrum of safe childbirth in relation to the above two issues [23]. According to the data of the Központi Statisztikai Hivatal (KSH - Hungarian Central Statistical Office) from 2006 the mothers' average age at delivery was 28.7 years of age, however, this increased to 29.8 years by 2017. The mothers' age at the time of the birth of their first child was also recorded on both occasions, this showed an age of 26.9 years in 2006, growing to 28 years in 2017 [30].

Further demographic factors may also be conducive to PB, i.e. marital status (being a widow, divorced, or single also increases the risk), socioeconomic status (level of education, employment situation, income, living conditions) [23].

In 65 to 70% of all PB cases, environmental and other negative factors contribute [23]. Amongst these some are exceptionally important, e.g. the mother's lifestyle, such as inadequate nutrition during pregnancy, possible nutritional deficiencies, extreme diets conducted without medical supervision, emaciation [31]. Low gestational body mass index brings forth a high risk of PB, whereas in the case of obese pregnant women the rate is lower, so obesity seems to provide some sort of protection from PB [32]. Notwithstanding, obese women face a higher risk of preeclampsia and diabetes, which, in turn, are associated with PB. Smoking, abuse of alcohol or drugs [33], application of certain - e.g. psychotropic - medications during pregnancy [34], exposure to chemical substances [35] or irradiation of the female pelvis [36], mental tension or exposure to objectively stressful situations (e.g. access to safe accommodation, serious financial problems) [33] all predispose to PB. A less explored area is that certain fathers may also be causes of PB in relation to the psychosocial aspects of pregnancy via their lifestyle and the health-related and mental impacts they have on their pregnant partners.

Further causes of PB are maternal internal illnesses like sugar metabolism disorders (insulin resistance, diabetes, gestational diabetes) [33], maternal overweight and obesity [33], maternal infections (sexually transmitted, vaginal, and genitourinary infections) [37, 38], hypertension [33], asthma [33], chronic cardiovascular [39], hepatic [40], pulmonary [33] and renal [41], autoimmune [42], cancer diseases [43] and psychiatric disorders [44].

Due diligence must be applied when treating vaginal inflammations and urinary infections (e.g. *Streptococcus agalactiae* [45], *Ureaplasma urealyticum* et *Mycoplasma hominis* [46], *Escherichia coli* et *Herpes simplex virus* [47]) as these may contribute to the development of

chorioamnionitis and premature rupture of the membranes. Intrauterine infections may be responsible for 25 to 40% of preterm births, according to microbiological studies [45].

Mercer et al reported that women with previous preterm delivery faced a 2.5 times higher risk of preterm delivery in their subsequent pregnancy [48]. Should the interval between two pregnancies not reach 6 months, this may double the risk of PB [49].

PB risk can also be elevated by previous spontaneous and/or induced abortion, or anatomic anomalies regarding the structure or position of the uterus that can occur as a result of benign alterations (e.g. myomas), development defects, previous surgeries performed on the uterus, or cervical insufficiency that can develop due to previous abortions. Cervical cone biopsy or loop electrocautery excision may lead to an increased risk of spontaneous PB, just like certain uterus anomalies, e.g. presence of septum [50]. Pregnancies not or insufficiently cared for, polycystic ovary syndrome (PCOS) [51], and thyroid gland dysfunctions [33] could also serve as predisposing factors.

Certain pregnancy-related conditions may also render the pregnant woman predisposed to PB, such as a strained uterus wall (e.g. due to multiple pregnancies), the placental anatomic, implantation, adhesion disorders (placenta praevia, placental abruption) and placental insufficiency [33]. Placental abruption or placenta praevia - caused vaginal bleeding is linked to a very high risk of PB. However, vaginal bleeding in the first and second trimesters not due to the above causes can also be connected to PB [52]. Preterm labour can also be associated with amniotic fluid volume extremes, i.e. polyhydramnion or oligohydramnion [33]. Genetic and developmental disorders of the fetus; fetal metabolic diseases; the fetus suffering from grave malnutrition in the uterus, atrophy of the fetus; intrauterine death of the fetus; intrauterine infection (often experienced premature rupture of the membrane) caused by chorioamnionitis; preeclampsia or eclampsia, also induction of delivery in case of miscalculating the GA may become predisposing factors [33].

The extension in the mother's age in relation to conception is remarkable, both in the case of the first child and the subsequent children and this may lead to impaired conception and increased chance of any illness of the mother, which can serve as a potential cause to PB and birth defects. Based on scientific data, pregnancies via assisted reproductive technology demonstrate a higher rate of preterm birth, since the women and men resorting to this option are of a higher average age, also their existing illness aggravating spontaneous conception can be a factor [53]. The majority of pregnancies via assisted reproductive technology are multiple pregnancies, also raising the risk of PB [54]. About 75% of preterm births happen spontaneously and 25% are medically induced for reasons concerning the mother or the baby [55].

Aside from the knowledge of the risk factors, it has to be acknowledged that in 25% of pregnancies ending in preterm births, the known factors cannot be identified [56].

#### 4.4. Connection between maternal periodontitis and preterm birth or discrepancies in the scientific literature

Galloway was the first (1931) to declare that the periodontium infected by Gram-negative anaerobic bacteria could have a harmful effect on the pregnant woman and the development of the fetus [3]. Romero et al noted in 1988 that infection is to be regarded as one of the main causes of PB with LBW, as is confirmedly responsible for it in 30% of all cases [57]. In the same year, Hillier et al concluded that the bacterial infection of the chorioamnion is connected with the histologically proven chorioamnionitis and both are strongly linked with PB [58]. It was also clear that in the cases of histologically proven chorioamnionitis identifying the bacteria was not successful in some of the examined placentas. This showed a contradiction and prompted the researchers to conduct examinations into how inflammation might have developed in the placenta without confirmed bacterial infection. According to the result of further research [3, 56, 59], infection can be situated somewhere in the body further away from the fetoplacental unit or the genitourinary tract. Such infections can be a risk of PB via either the indirect effect of translocated bacterial products, e.g. lipopolysaccharides (LPS) or the mechanism of action of the inflammatory mediators produced by the mother's body.

After Galloway's research, Offenbacher et al also highlighted the potential connection between periodontal status and PB in their study (1996). They assumed that the oral cavity infection (e.g. chronic periodontitis) might serve as a reservoir for inflammatory mediators, posing as a potential threat to the placenta and the fetus, enhancing the chance for PB [3]. Subsequently, more and more statements on similar subjects were published [60, 61]. Meanwhile, other studies seemed to prove that maternal urinary infection can be linked to the increased prevalence of preterm births [38].

There were animal experiments carried out at the beginning of the 1990s in order to gain information on the link between maternal infection and adverse obstetrical outcomes. In several studies, golden hamsters were used as test subjects. These studies succeeded in proving the theory according to which infections developing in the body far away from the pregnant uterus may contribute to PB. Collins et al found that the further, non-disseminating infection of the bacteria *Porphyromonas gingivalis* or the experimentally induced periodontitis may cause complications in the pregnancy of golden hamsters [62].

Several animal experiments, epidemiological research, systematic analysis, and meta-analyses have been published in order to reveal this connection [3, 63]. Since then, the examination of the intensity of gingival bleeding, the probing depth (PD), and the inflammatory processes in the oral cavity (the latter on both bacterial and molecular levels) are viewed from a new perspective, as a connection was assumed between the above factors - via their impact on the pregnant uterus - and the prevalence of PB. Progressively more evidence proves that chronic periodontitis may be a risk factor in PB, hence interventional studies examined the effect of treating periodontal diseases during pregnancy on the likelihood of PB.

The first statement related to the periodontal treatment of pregnant women was published in 2001 by Mitchell-Lewis et al. In their research, the prevalence of PB showed a declining trend due to the periodontal treatment, however, they did not succeed in confirming a significant difference between the treated and the control group [64]. Lopez and colleagues (2002) identified periodontal disease as an independent risk factor in PB with LBW. They found during their research that the periodontal treatment of those gravidas suffering from periodontal diseases significantly lowers the risk of preterm births with LBW [65].

Xiong et al arrived at inconsistent results when systematically reviewing 25 studies on the subject in 2006. The research focused on PB with LBW, LBW, PB, BW across gestational ages, miscarriage, and preeclampsia. Of the studies, 18 implied a connection between periodontal disease and PB, but 7 did not find the link. Three clinical research suggested that oral prophylaxis and periodontal treatment may reduce the occurrence of preterm births with LBW and preterm births [66]. Michaelowicz et al found during their research that treating periodontal diseases of pregnant women did help the periodontal problem and was safe to carry out, however, it did not significantly change the rate of preterm births, LBW, or fetal growth restriction [67].

Vergnes and colleagues published the results of their work in 2007: they carried out a meta-analytical review across 5 medical databases (MEDLINE, EMBASE, LILACS, BIOSIS, and PASCAL), regarding studies that linked PB and/or LBW with the maternal periodontal diseases. In their review, 17 studies conformed to their selection criteria. There were 7151 pregnant women taking part in the studies, with PB and/or LBW occurring in 1056 of the cases and their results suggested a likely connection [68].

Radnai and colleagues carried out an interventionalist research (2009) with the aim of analysing the effect of periodontal treatment in cases of threatening PB or pregnant women suffering from starting local chronic periodontitis. According to their results, in the case of treated patients the occurrence of PB and LBW was significantly lower than in the untreated control group [69].

In their study of 2013, Sanz and Kornman arrived at the conclusion that even though periodontal therapy proved to be safe and improved the periodontal status of pregnant women, the case-specific periodontal therapy did not lower the rate of preterm births or low birth weights with or without systemic antibiotics [70].

A systematic and meta-analysis carried out in 2019 confirmed significantly that the periodontal treatment during pregnancy lowers perinatal mortality and the risk of PB, at the same time, however, it increases the newborns' BW [63].

It occurred among the published studies that the statistical samples were not representative, the gravidas taking part in the study belonged to different ethnic groups, had different social backgrounds, were not selected according to the same criteria or there might have been a divergence in defining periodontitis or other important factors (e.g. undesirable obstetrical outcomes). Despite some studies providing convincing evidence, the heterogeneity of the available scientific literature prevents drawing a solid and definitive conclusion.

As emphasised by the authors of various studies published in the field - more thoroughly prepared, methodologically uniform, well structured, and comprehensive epidemiologic and interventional research would be needed to prove the connections highlighted in the available studies.

#### 4.5. The role of periodontopathogenic bacteria in the development of periodontal diseases

According to the up-to-date data of the expanded Human Oral Microbiome Database there are 774 bacterial species in the oral cavity [71], the bulk of them are harmless, commensal microorganisms constituting the normal flora. The health-associated biofilm constitutes of *Neisseria*, *Streptococcus*, *Actinomyces*, *Veillonella* and *Granulicatella* bacteria species [72]. Aside from these, the pathogen microbes are present mostly in a low number. The shift in the rates of the normal flora towards the pathogen bacteria (dysbiosis) leads to the appearance of a bacterial microflora that induces a dominant immune response harming the body [73]. Among these microbes it is most often the obligate or facultative anaerobic Gram-negative ones, e.g. *Aggregatibacter actinomycetemcomitans*, *Fusobacterium nucleatum*, *Porphyromonas gingivalis*, *Tannerella forsythia*, *Treponema denticola*, *Prevotella intermedia*, *Filifactor alocis* and *Campylobacter rectus* are the ones behind the periodontal diseases [74, 75].

In the case of a healthy individual, the ratio of pathogen phyla in the oral cavity is low or the immune system is still capable of neutralising strong negative impacts. Should the balance between the organism and the bacterial microflora overturn, it would enable the development

of the periodontitis in itself. The amount of bacteria in the dental plaque may reach the  $1-2 \times 10^{11}$  per gram on and/or under the marginal gingiva. Further to the above, it was demonstrated that the bacteria can penetrate the periodontal pocket tissues [76].

The size of the surface through which the bacteria may access the tissues is significant. The bacteraemia lasts a short period (15 to 30 minutes) only, still, it reoccurs at every brushing of the teeth [76] or chewing on a tougher piece of food, even for decades or at the events of dental interventions (e.g. tooth extraction).

In pregnancy, due to the changes in the gingival tissue, the gingiva is less resistant to the bacteria and their products. The first symptoms of gingivitis develop in the second month of pregnancy [77]. In case of gingival inflammation, if dental plaque is also present the symptoms are more serious. Apart from the presence of the dental plaque or existing inflammation, during pregnancy the gingiva is more prone to bleeding [78]. If the inflammation exists permanently, becomes chronic, and develops into periodontitis, the inflammation triggered by the Gram-negative bacteria affects the periodontium, i.e. the gingiva and the alveolar bone, too. In this case, the periodontal pocket can be considered a reservoir for the Gram-negative bacteria.

#### 4.6. The potential pathomechanism of the connection between periodontal diseases and preterm birth

##### 4.6.1. Scientific exploration in search of the potential pathomechanism

Offenbacher et al investigated prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) and interleukin (IL)-1 $\beta$  levels in the gingival crevicular fluid (GCF) of pregnant women. They observed that in the case of gingivitis, the amount of GCF increases and they could detect inflammatory mediators in it. The PGE<sub>2</sub> level was significantly higher in the sulcus fluid in the case of mothers having had a PB as opposed to those with newborns with normal BW. The elevated PGE<sub>2</sub> level as the marker of periodontal disease could be linked to declining BW. Similarly, the examined bacteria (*Bacteriodes forsythus*, *Porphyromonas gingivalis*, *Actinobacillus actinomycetemcomitans* and *Treponema pallidum*) can be found in a higher amount in the oral cavity of mothers with preterm births [79].

These authors identified an immunoglobulin M (IgM) antibody produced specifically against the periodontopathogenic bacteria, in the fetal serum. This proved to be direct evidence that the bacteria and/or their products can reach the fetoplacental unit and crossing the placental barrier pose a systemic challenge to the fetus [80]. Based on these results Offenbacher set up a model



for PB linked with periodontal infection, the essence of which is that the periodontitis caused by the infection of Gram-negative bacteria operates as a remote chronic infection that results in lipopolysaccharides and inflammatory mediators entering into the systemic circulation. A possible way for the remote infection to spread is that some of the periodontal pathogens penetrate the host tissues. The lipopolysaccharides, entering the placenta, elicit a fetal immunological and inflammatory response. Due to the effect of the bacteria and their products, inflammatory mediators such as PGE<sub>2</sub>, IL-1 $\beta$  and tumor necrosis factor alpha (TNF- $\alpha$ ) are released locally from the maternal and fetal (decidual, chorioamniotic) tissues, thus causing uterus contractions, cervical dilatation, and PB [79, 81].

Madianos et al detected in 2001 that the lack of the maternal IgG antibody produced against several oral pathogens could be linked with the increased prevalence of PB. They arrived at the conclusion that those pregnant women suffering from periodontitis who lacked protective maternal antibody response could be linked with the dissemination of oral pathogens that once passing into the fetus may lead to PB [82].

#### 4.6.2. Direct and indirect mechanisms

Regarding the potential pathomechanism of the connection between periodontal diseases and PB, two main paths have been identified in the last years. The periodontopathogenic bacteria reach the fetoplacental tissues and the amniotic fluid where they trigger a secondary infection, local immune response, and inflammation (chorioamnionitis) via direct mechanism: from the deeper tissues more permeable due to the periodontitis, the periodontal pockets via haematogenous dissemination [83]. In the case of patients with healthy periodontium the periodontal sulcus area is approximately 5 cm<sup>2</sup>, however, with periodontitis, this surface can reach 8-20 cm<sup>2</sup> [84]. Chronic periodontitis means that the 4-5 mm deep periodontal pockets around the teeth together with the damaged epidermis of the pockets provide an about palm size open wound surface through which the obligate anaerobic, endotoxin-producing bacterial colony - among others - is in contact with the body [85].

The essence of the indirect mechanism is that inflammatory mediators (intermediates, cytokines) are released from the chronically inflamed periodontium into the systemic circulation. These cause a secondary inflammation in the fetoplacental unit, either directly or indirectly by inducing an acute phase reaction in the gravida's liver via the expression of acute phase proteins (C-reactive protein, CRP and fibrinogen) [86].

During pregnancy, the inflammatory response is strongly activated [87], attested by the increased expression of the inflammatory markers [88]. Both the chorioamnionitis arising from local immune response and the inflammatory mediators that reach the fetoplacental unit via haematogenous dissemination have an impact on the metabolism of the fetoplacental unit [89]. The increased production of proinflammatory cytokines and lipid mediators happens either on the site of the infection (i.e. the periodontium) or as a result of the placenta's response to the infection. The proinflammatory cytokines, especially the IL-1, IL-6, TNF- $\alpha$  stimulate the PGE<sub>2</sub> production by the placenta and chorioamnion. Prostaglandin assists the physiological regulation of the pregnancy, administering medicine containing prostaglandin leads to abortion or delivery [56]. The toxins of the circulating microbes, as well as their toxic metabolites cause direct histological toxicity.

The physiologic cytokine-production (especially the IL-1 $\alpha$ , IL-6 and TNF- $\alpha$ ) of the chorion and through this the anomalous induction of PGE<sub>2</sub> can lead to early uterine activity, the shortening and dilatation of the cervix, the rupture of the amniotic membrane thus to threatening or actual PB [90].

#### 4.7. Adequate examination practices in relation to periodontitis

Approximately 41% of pregnant women report gingival bleeding when brushing their teeth [1]. This fact directed our attention to this recurrent symptom. The diagnostic option suitable to investigate and classify periodontal diseases is observing the PD next to the dental cervix and the possible bleeding on probing (BOP) during the examination. Should bleeding occur in the case of any given tooth, this information is noted in the records of that particular tooth.

The sulcus bleeding index (SBI) is a ratio expressing the rate of the teeth with gingival bleeding during probing (hereafter referred to as BOP teeth) to the total of the examined teeth.

## 5. Aims

Our research aimed at determining the periodontal status of the involved pregnant patients in the second trimester, and exploring the possible relationship between the presence of gingivitis, periodontitis, and the GA at delivery and the neonatal BW. We further investigated the possible connection between the GA at periodontal screening and the SBI, and its effect on the obstetrical outcome.

## 6. Material and methods

### 6.1. Materials and apparatus

This prospective clinical study was conducted at the University of Szeged, Department of Obstetrics and Gynecology. Szeged is the county seat of Csongrád-Csanád County, with a population of about 159,000 inhabitants. The Department of Obstetrics and Gynecology, a part of Albert Szent-Györgyi Medical School, is a state-financed unit and the only one where childbirth (about 2500/year) takes place in this city. This department is also responsible for complicated cases and cooperates with the NIC belonging to the Department of Pediatrics and Pediatric Health Center located at the Department of Obstetrics and Gynecology. It is also a regional center overseeing cases from the Southeastern region of Hungary. The study was conducted in cooperation with the University of Szeged Faculty of Dentistry Department of Prosthodontics. The study period for the periodontal examinations was between 1 August 2019 and 29 February 2020.

It is important to know that, in Hungary, all pregnancies that finish with deliveries are recorded in the electronic national health system database. Dental examinations are mandatory during pregnancy and the fact of the completed examination is recorded in the patient's Health Booklet, which follows an expectant woman from the start to the end of her pregnancy.

A dental unit had been installed at the department as part of the authors' previous research program and was used for this research, too. The examinations of the selected pregnant patients were carried out here by experienced dentists. Members of the study group were chosen from the patients provided with prenatal care at our department. The patients received information on the possibility of taking part in periodontal examinations at our department when booking an appointment for their first genetic screening (advised to be carried out at the 12th gestational week). Patients were selected for the research after completing this screening. They were offered the schedule of the periodontal examinations, so that they could book appointments at their convenience. Altogether 2860 ultrasound screenings were carried out during these 7 months, 1144 on inhabitants of Szeged.

A total of 111 healthy primigravida-primiparous pregnant women without significant illnesses were involved in this study which was ethically approved by the Ethical Committee of the Albert Szent-Györgyi Clinical Centre, Szeged, Hungary (approval number 123/2019-SZTE). Only inhabitants of Szeged who planned to give birth at our department were selected to take part in this study so that the prenatal care could be carried through including regular checkups

on patients and the periodontal examinations were easily accessible for them. The pregnancies and the health status of the patients were monitored until giving birth. The health status of all 111 patients was monitored throughout their pregnancies; all women gave birth at our institution. The patients were fully informed about the aim of this study, and they took part voluntarily after signing a written consent form.

## 6.2. Method

Periodontal examinations were performed after the ultrasound screening - that recorded the GA - by a dentist in the above-mentioned dental unit, according to the WHO guidelines. The examination methods are adequate and up to date with professional standards. An in-depth examination was carried out including an assessment of dental plaque accumulation, measurement of PD, and the detection of BOP possibly appearing as a result of probing.

The PD was recorded between the marginal gingiva and the deepest point of the sulcus or periodontal pocket. PD and BOP was used to determine the periodontal status of the patients, using a periodontal probe. The diameter of the probe tip used was 0.5 mm. For each tooth the PD was measured at six sites, these were: the mesiolingual, midlingual and distolingual sites, also the mesiobuccal, the midbuccal and the distobuccal ones. The only exceptions from the probing were the wisdom teeth. During the probing, the BOP was recorded for each site where the PD had already been determined. The BOP recording involved a 15 seconds observation period and then a record of the emergence of the bleeding on a Yes/No scale. Any recorded bleeding was then linked to the examined tooth (BOP tooth).

For each patient, the dentist's examination also included a thorough education on the correct oral hygiene regime including the use of toothbrush and dental floss. Those patients with a sulcus depth between 1-3 mm with no detectable bleeding in the gingiva were classified as periodontally healthy. Those with the same PD, but with a BOP  $\geq 25\%$  were identified as patients with gingivitis, and finally those patients with a PD  $\geq 4$  mm recorded for at least one site and a BOP  $\geq 50\%$  (of the teeth) were described as patients with periodontitis. PD and BOP are accepted as the most significant periodontal parameters and these were used to determine the periodontitis.

The above parameters were selected upon previous clinical practice and scientific studies. PD value of 4 mm is the threshold of dividing „critical PD” which covers PD values at or over 4 mm from the normal values which are smaller than 4 mm.

After the completion of the above periodontal examinations, the recruited patients were divided into 3 groups, namely: Healthy (H), Gingivitis (G) and Periodontitis (P), according to the periodontal status diagnosed during pregnancy. In our research, we use the term SBI as defined by the quotient of BOP teeth and the total number of examined teeth in each patient's case. After the deliveries, GA at delivery and neonatal BW were analysed and paired with the data of the patient's previous periodontal status.

### 6.3. Statistical analysis and graph editing

The statistical samples were characterised as the mean and standard deviation (SD) of the data, where the group means were compared by a one-way ANOVA (Analysis of Variance) formula, which can be considered a generalisation of the Student's two-sample t-test for more than two groups. Pearson's correlation coefficient and the regression line were also used to examine the linear relationship between the examined variables. The p-value (p) describing the significance of the correlation was also supplied. According to this,  $p < 0.05$  value was accepted as statistically significant and the statistical analyses were carried out using the program of SPSS V26 (Statistical Package for Social Sciences Version 26). The Microsoft Excel program was used to edit the graphs.

## 7. Results

### 7.1. The gestational age at periodontal examination, gestational and maternal age at delivery and birth weight at delivery

The GA at the dental examination, the gestational and maternal ages at delivery, and the BW at delivery are presented in Table 1. The 111 patients were classified into 3 categories based on the results of the measurements detailed in section 6.2: 17 healthy individuals (H), 67 patients with gingivitis (G), and 27 patients with periodontitis (P). The 'N' represents the number of the patients. Data regarding GA at periodontal examination, GA at delivery, maternal age at delivery and BW was recorded in each group during the examinations and then compared across the groups and hence across the bleeding frequencies specified in the definitions given above.

A negative correlation can be noted between the birth weights of the 3 examined groups and the increase in the group-specific BOP prevalence, however, as seen in Table 1, the correlation is statistically non-significant.

Table 1. Sample characteristics in different periodontal status groups

	<b>Healthy (H)</b> <b>N = 17</b>	<b>Gingivitis (G)</b> <b>N = 67</b>	<b>Periodontitis (P)</b> <b>N = 27</b>	<b>ANOVA</b> <b>(p)</b>
<b>Gestational age (week) at dental examination</b>	16.24 ± 3.492	15.00 ± 3.516	14.00 ± 3.150	0.111
<b>Gestational age (week) at delivery</b>	38.53 ± 1.772	39.07 ± 1.454	38.67 ± 1.414	0.253
<b>Maternal age (year) at delivery</b>	31.25 ± 4.337	30.91 ± 5.197	29.53 ± 6.309	0.464
<b>Birth weight (gram)</b>	3518.82 ± 548.212	3402.24 ± 541.443	3396.67 ± 611.826	0.726
Analysis of Variance (ANOVA)				

Results are shown as means ( $\pm$  SD). The detected difference in the examined groups' records for birth weight was determined as statistically non-significant.

## 7.2. Comparison of gestational age at periodontal examination in different status groups

The GA at the time of attending the periodontal examination was recorded at the examination and then analysed in all status groups. The results are shown in Table 2.

Patients in group P had the highest GA at the time of the periodontal examinations. It is worthy to note that the number of healthy patients amongst those taking part in the survey was substantially low (15.3% of the total patients).

Table 2. Gestational age (week) at periodontal examination in different status groups

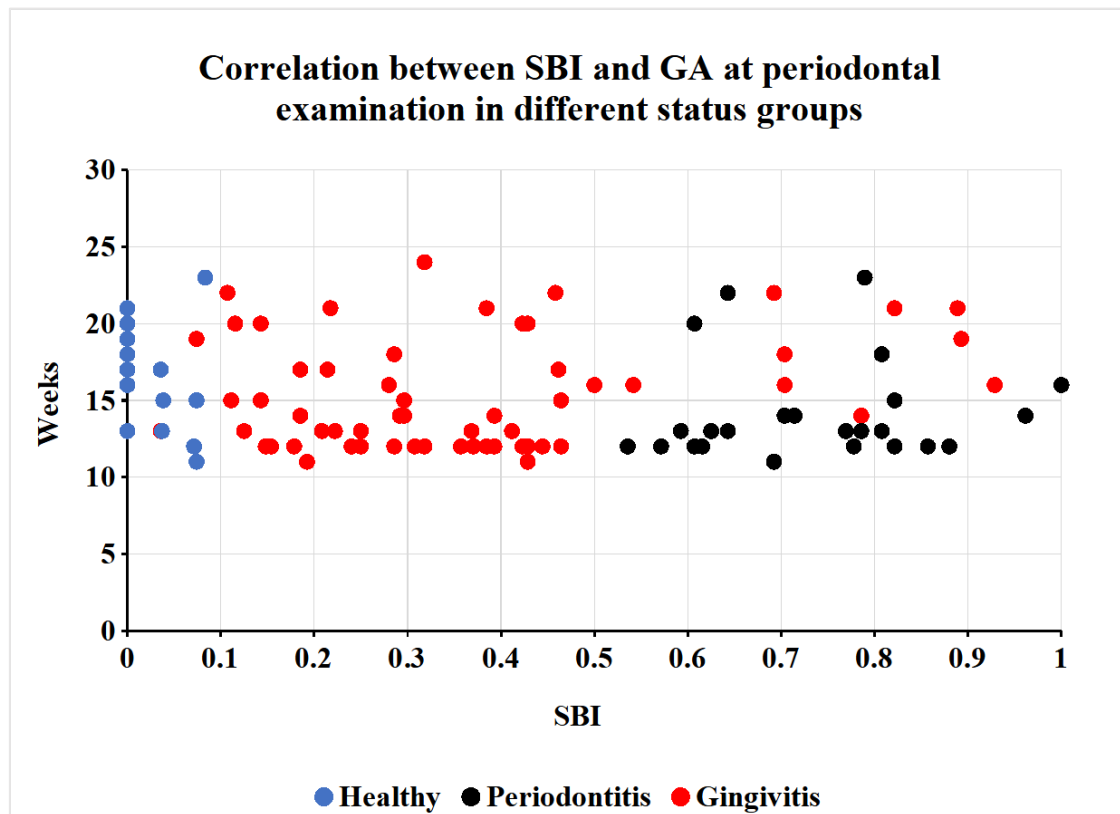
<b>Group</b>	<b>N</b>	<b>Mean (SEM)</b>
<b>Healthy</b>	17	14.00 (0.764)
<b>Gingivitis</b>	67	14.95 (0.423)
<b>Periodontitis</b>	27	15.00 (0.677)
ANOVA p = 0.111      SEM = standard error of the mean		

Patients in group P had the highest GA at the time of the periodontal examinations however, the correlation is statistically non-significant;  $p < 0.05$  was considered statistically significant. There were relatively few patients who could qualify as 'healthy' (15.3% of the total number of patients).

### 7.3. Correlation between sulcus bleeding index and gestational age at periodontal examination in different status groups

The SBI indices are summarised in Figure 1. According to our findings, the patients in group H attended the periodontal examinations at a lower GA. In the case of periodontitis, the GA at the time of the periodontal examination was higher, but this correlation proved to be statistically non-significant.

Figure 1. Correlations between sulcus bleeding index and gestational age at periodontal examination in different status groups



Results are shown as means ( $\pm$  SD). GA = gestational age; SBI = sulcus bleeding index;  $n = 111$ ; and  $p < 0.05$  was considered statistically significant.



#### 7.4. Correlation between sulcus bleeding index and gestational age at periodontal examination in the Gingivitis group

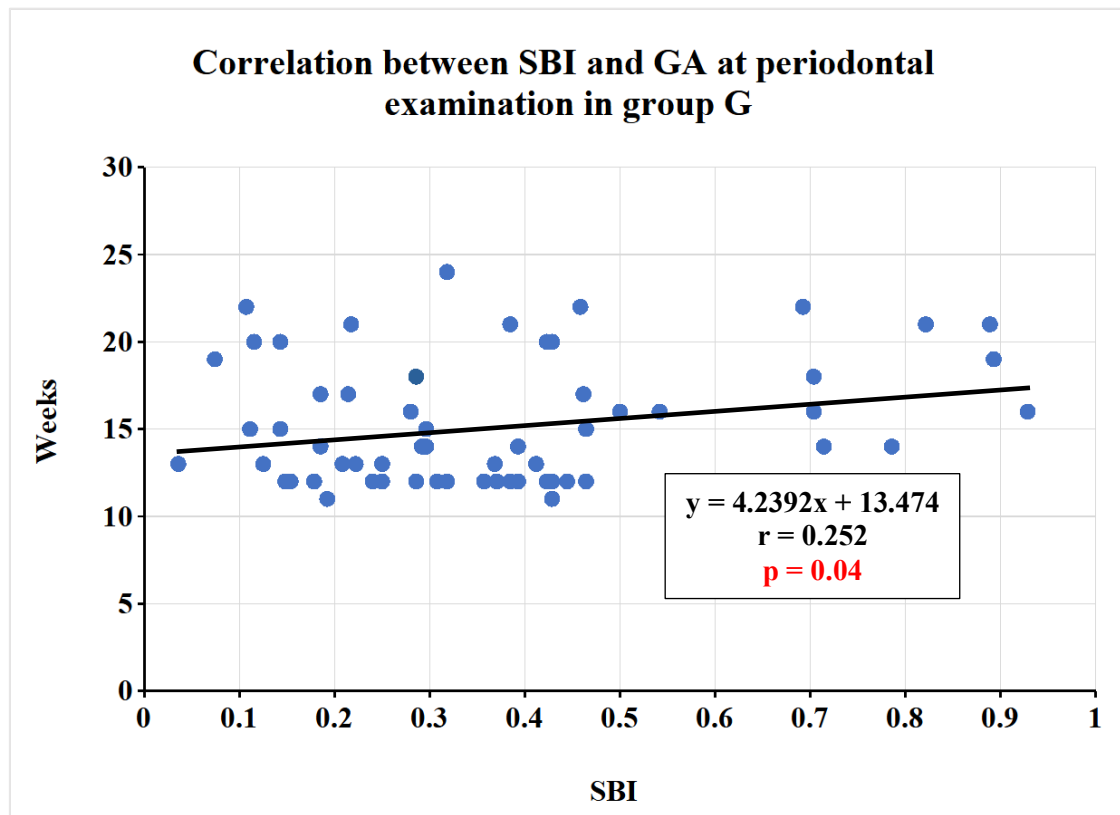
In group G a significant positive correlation was found between the SBI and the GA of the patients at periodontal examination, where the correlation coefficient, i.e.  $r = 0.252$  and  $p = 0.04$ . This means that those patients who suffered from an increased SBI attended the periodontal examinations at a significantly higher GA. The data demonstrating the above correlation is shown in both Table 3 and Figure 2, also presenting the G rate recorded at the time of attending the periodontal examination.

Table 3. Correlation between sulcus bleeding index and gestational age at periodontal examination in different status groups

<b>Group</b>	<b>N</b>	<b>Correlation coefficient (r)</b>	<b>p-value (p)</b>
<b>Healthy</b>	17	-0.391	0.120
<b>Gingivitis</b>	67	0.252	<b>0.04</b>
<b>Periodontitis</b>	27	0.127	0.527
<b>Total</b>	111	-0.035	0.714

Significant positive correlation between SBI and patients' GA at the periodontal examination in group G;  $p < 0.05$  was considered statistically significant.

Figure 2. Correlation between sulcus bleeding index and gestational age at periodontal examination in the Gingivitis group

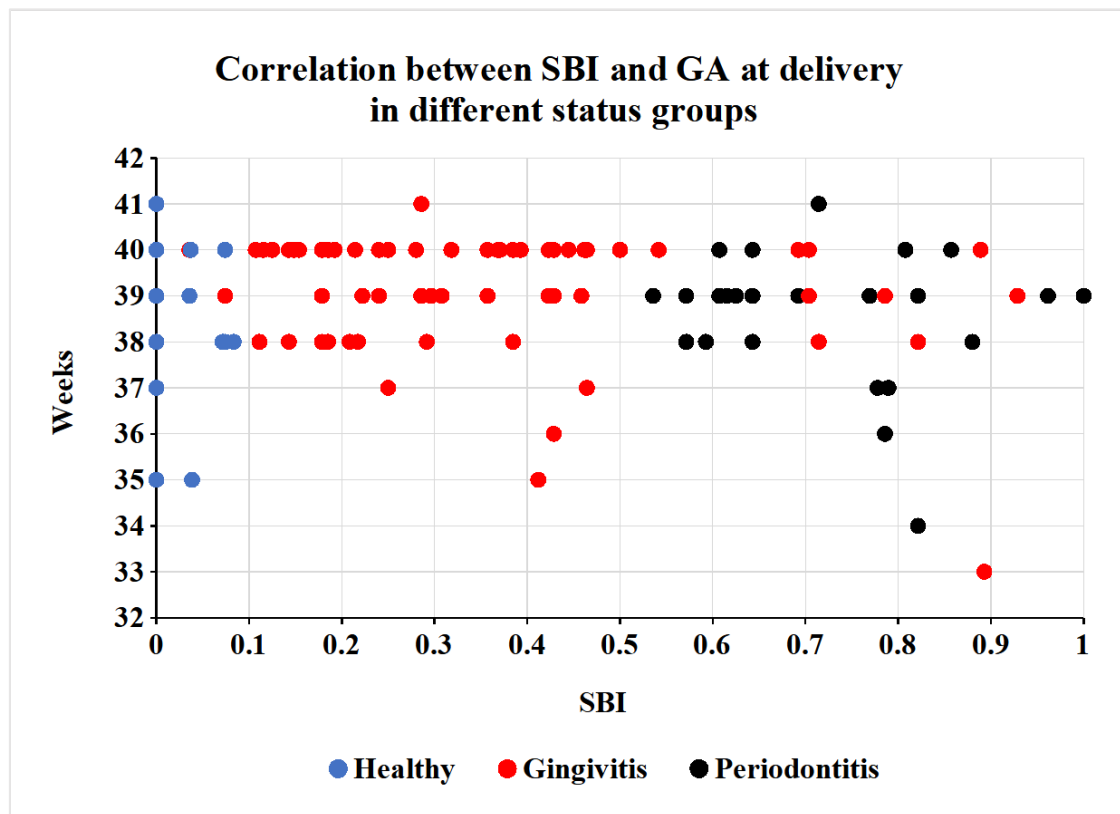


Results are shown as means ( $\pm$  SD). G = gingivitis; GA = gestational age; SBI = sulcus bleeding index;  $n = 111$ ; and  $p < 0.05$  was considered statistically significant.

### 7.5. Correlation between sulcus bleeding index at periodontal examination and gestational age at delivery in all groups

Further to the above analysis we examined the data regarding the delivery for each patient. This included the correlation between the SBI at periodontal examination and the GA at delivery. In the case of a higher SBI the GA at delivery proved to be lower (Figure 3).

Figure 3. Correlation between sulcus bleeding index at periodontal examination and gestational age at delivery in different status groups

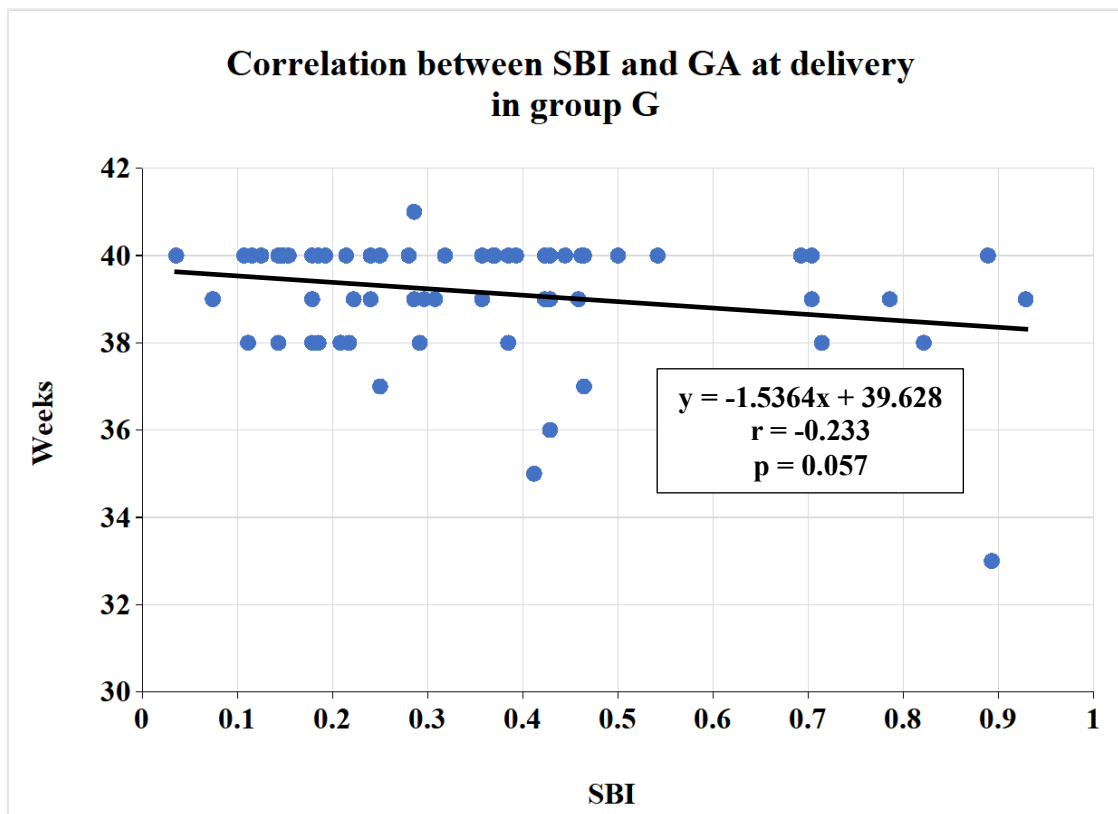


Results are shown as means ( $\pm$  SD). GA = gestational age; SBI = sulcus bleeding index; n = 111; and  $p < 0.05$  was considered statistically significant.

### 7.6. Correlation between sulcus bleeding index at periodontal examination and gestational age at delivery in the Gingivitis group

Having conducted a statistical analysis, we found a negative correlation in group G, i.e. the higher the SBI was for a patient, the lower was the GA at delivery. The correlation is just about non-significant statistically (Figure 4) in this group. The results are shown in Table 4.

Figure 4. Correlation between sulcus bleeding index and gestational age at delivery in the Gingivitis group



Results are shown as means ( $\pm$  SD). G = gingivitis; GA = gestational age; SBI = sulcus bleeding index; n = 111; and  $p < 0.05$  was considered statistically significant.

Table 4. Correlation between sulcus bleeding index at periodontal examination and gestational age at delivery in different status groups

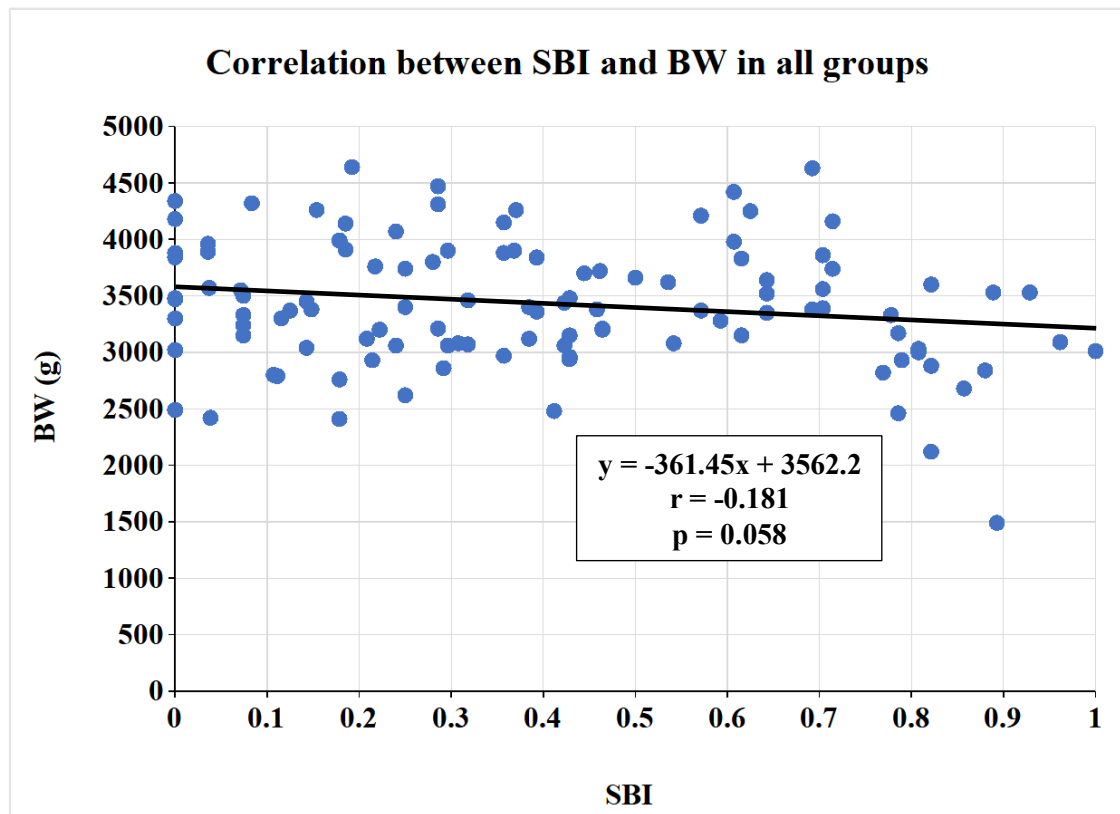
<b>Group</b>	<b>N</b>	<b>Correlation coefficient (r)</b>	<b>p-value (p)</b>
<b>Healthy</b>	17	-0.120	0.647
<b>Gingivitis</b>	67	-0.233	<b>0.057</b>
<b>Periodontitis</b>	27	-0.142	0.480
<b>Total</b>	111	-0.120	0.21

We found a negative correlation in group G, the higher the SBI of a patient was, the earlier she delivered her baby. This correlation did not qualify as statistically significant, but only barely missed the threshold;  $p < 0.05$  was considered statistically significant.

### 7.7. Correlation between sulcus bleeding index at periodontal examination and birth weight in different status groups

We analysed the relationship between the SBI and the BW. Regardless of the periodontal status we observed a negative correlation (Figure 5), i.e. with the growing level of SBI the newborns' BW seemed to decrease, however, this correlation was just about non-significant. The correlation coefficient is  $r = -0.181$  at the p-value of 0.058, which is just below the level of statistical significance.

Figure 5. Correlation between sulcus bleeding index and birth weight in all groups

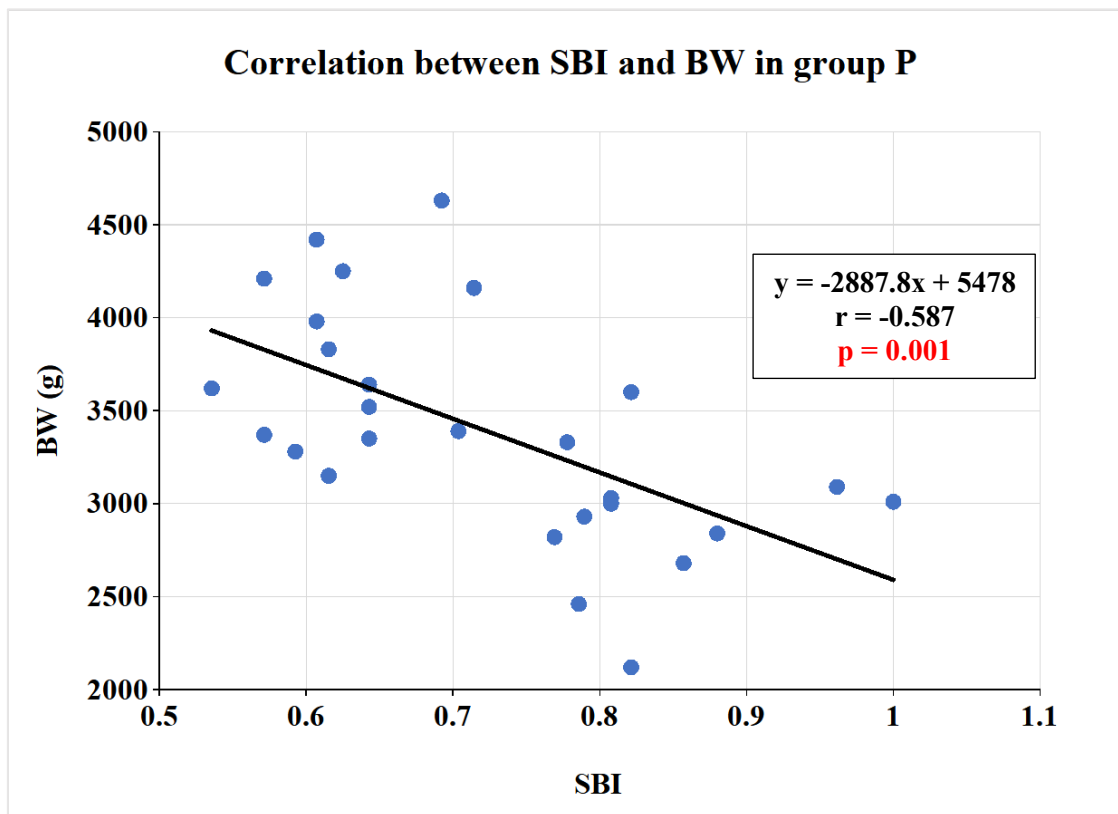


Results are shown as means ( $\pm$  SD). BW = birth weight; SBI = sulcus bleeding index;  $n = 111$ ; and  $p < 0.05$  was considered statistically significant.

### 7.8. Correlation between sulcus bleeding index and birth weight in the Periodontitis group

After a further investigation of these data, it was clearly visible that the correlation was the most pronounced and statistically significant in group P, in which a significantly lower newborn weight was observed with an increase in SBI. This means that a more severe periodontal disease was associated with a lower BW ( $r = -0.587$ ,  $p = 0.001$ ). The data are presented in Figure 6.

Figure 6. Correlation between sulcus bleeding index and birth weight in the Periodontitis group



Results are shown as means ( $\pm$  SD). BW = birth weight; SBI = sulcus bleeding index; P = periodontitis;  $n = 111$ ; and  $p < 0.05$  was considered statistically significant.

## 8. Discussion

### 8.1. Relationship between oral hygiene during pregnancy and obstetrical outcomes

Infections affecting the whole body may be linked to preterm births, however, we haven't had information on these links before. Most often urogenital, vaginal, and sexually transmitted infections have been examined for potentially causing pregnancy complications. Since then it occurred that organs further away from the target organ of pregnant uterus might be significant in causing infections, e.g. the subgingival microorganisms related to oral inflammatory processes responsible for varied periodontal diseases.

Recently, an increasing number of research has been conducted into the relationship between oral hygiene during pregnancy and obstetrical outcomes [63]. Over the course of a prospective analysis, the authors examined the link between the maternal periodontal status, the oral cavity burden and the CRP level of the serum and the newborn baby's BW, and arrived at the conclusion that the deteriorated maternal periodontal status, the increased oral cavity burden and the escalated systemic inflammation may have a pernicious effect on the BW [91].

Inappropriate oral hygiene is identified as the main contributing factor causing periodontal diseases such as gingivitis or periodontitis. Pregnancy-induced hormonal changes, the increased inflammatory and immune system response common during pregnancy may result in an elevated risk of contracting periodontal diseases in this period or the intensification of periodontal diseases already present at conception, also it may result in negative obstetrical outcomes.

Our research underlines the relevance of periodontal screening during pregnancy, conjoining previous studies drawing attention to the impact that oral hygiene and the adequate treatment of the periodontal diseases has a positive effect on the obstetrical outcome [63]. The methods and the results of our present research correspond to the data of international research: during periodontal examinations the PD and the BOP are widely accepted as the most significant parameters, adequate examination practices to diagnose and state the severity of the periodontal diseases (staging) [60, 61, 69], and it is known from previous studies that the increasing trend of BOP (and the calculated SBI) can be linked to the threatened preterm births and preterm births [61, 92].



## 8.2. Reasons for the belated detection of periodontal diseases amongst pregnant women

Even though the obstetrical protocol refers to the periodontal screening and treatment of pregnant women, it is substantially unknown amongst them. Many patients underestimate the significance of gingival bleeding during brushing their teeth. They do not consider it important and/or are afraid of the dental checkup, so avoid the assumingly unpleasant examination [1]. Our research show that the pregnant women with dental problems attended periodontal examinations at a higher GA. The increasing frequency of gingival bleeding experienced while brushing teeth, the deteriorating dental status may lead to anxiety about the dental checkup, and may explain why some patients only attend these checkups after some delay. Both quantitative and qualitative studies regarding this issue have corroborated that women may have fears of dental examinations during pregnancy [93].

The average proportion of registered pregnant women across Hungary undergone dental screening as part of the primary care was 15.5% in 2001, the lowest recorded in county Nógrád (10.3%), the highest in county Baranya (24.8%). In the following year this proportion grew by 3.9% [2]. Battancs et al conducted research at University of Szeged, Department of Obstetrics and Gynecology among 275 pregnant patients cared for by the Department and recorded via questionnaire that 72.2% of the patients had taken part of dental screening. The outstandingly high proportion was explained by the authors with the facts, that Szeged is a university town, the majority of patients were local or from nearby areas, and a fair amount of those completing the questionnaire had received higher education (50.4%) and worked in intellectual professions (53.2%). This data indicates that individuals' oral care habits, and their tendency to attend dental checkups vary remarkably by geographical area, level of education, financial situation, and several further personal factors [1].

An important feature of our research is that there were relatively few patients taking part in our survey who could qualify as 'healthy' (15.3% of the total number of patients), and this highlights the importance of periodontal care before conception for women planning pregnancy. There may be many factors behind this pattern, but most of the time, it is due to a previous negative experience or a lack of education regarding oral hygiene. During pregnancy, the inclination to anxiety and the heightened focus on emotions can increase the perception of pain at dental examination and treatment [94].

### 8.3. Research data

The results of our research showed a significant correlation between P and a low BW at delivery ( $p = 0.001$ ). This means that those gravidas with a higher BOP - and consequently the calculated SBI - were facing a higher risk of their newborns being born with a lower BW. The same results did not demonstrate a connection between the poor dental status and premature delivery (Table 1), however.

Any deliveries after the 37th week were identified as at-term births. Deliveries between the 24 weeks 0 days and the 36 weeks 6 days dates were identified as preterm deliveries. If the weight of the newborn was under the 5th percentile, it was classified as low BW.

Our results were in accord with the scientific literature regarding the role of hormonal and inflammatory processes when it comes to periodontal disease leading to premature birth. Oral microorganisms release endotoxins and cytokines and this process is responsible for prompting the inflammatory cascade resulting in molecular processes that may lead to PB [70].

Further to the BW, the GA at the time of the periodontal examination was also found to be correlated with BOP. The value of  $p = 0.04$  shows the significant correlation found in the Gingivitis group between the SBI and the GA of the patients at the time of the periodontal examination. Our observations in group G confirmed that BOP and the GA at the periodontal examination had a positive correlation which also suggests how important periodontal screening is during pregnancy. Concluding the above it was clearly demonstrated how an insufficient periodontal status during pregnancy has a negative impact on the obstetrical outcomes.

The fact that each patient involved in our research had undergone a detailed and thorough periodontal examination followed by a close inspection of the gravidas up until the delivery and gained accurate data on the GA at delivery and the BW, add to the integrity of our research. The correlation between the SBI and GA at delivery in group G (Figure 4) and the BW in all groups (Figure 5) almost reached the level of statistical significance, but failed to do so, which might be explained by the relatively low number of cases, as a methodological limitation to this study. The low number of patients was caused by the onset of the COVID-19 (Coronavirus disease 2019) pandemic, which stopped study-related dental examinations, as these would have meant an increased risk to both our patients and the professionals carrying out the periodontal screenings.

We suspect that with a higher number of patients involved in our research, we could have produced statistically significant results regarding the correlations between the SBI and the GA

at delivery, and the BW. Unfortunately the patient number was not sufficiently high to allow differentiating between preterm births depending on the severity of prematurity (late, moderate, very preterm, or extremely preterm), as referred to in section 4.3.1, or to observe any possible connection with the periodontal status of the mothers.

The remarkable connections observed regarding the significance of a correct oral hygiene regime during pregnancy inspired us to conduct further research into this subject.

#### 8.4. The relevance of adequate oral hygiene

In our experience, providing the necessary information for our patients was successful in each case, and the patients were readily willing to take part in our research. It is important to note that even though the periodontal examinations were thorough and required calm cooperation, based on the feedback received from them, no one found the examinations unpleasant or unbearable.

A strong correlation was proved to exist between the maternal periodontal status and the obstetrical outcomes highlighting the significance of oral health. We can say that preventive oral care before and during the pregnancy is critical from both the mothers' and the newborns' perspective [95]. This observation stresses the importance of dentists and obstetricians collaborating. Educating women in the correct oral hygiene regime is crucial in the prevention of pregnancy-associated complications like neonatal LBW or prematurity.

Several publications draw attention to the importance of dental screening before and during pregnancy [95, 96]. On one hand, adequate education and care are of utmost importance, since the dental status at the beginning of the fertile age does matter. On the other hand, the willingness to attend dental checkups regularly is low among the Hungarian population [1]. Acquiring the correct oral hygiene practice is indispensable, especially regarding interdental surfaces. It is recommended to use toothpaste for gingivitis and - considering the tendency of increased gingival bleeding during pregnancy - a fine or medium bristle-strength toothbrush, ideally an electric one to remove plaque more effectively. Using soft dental floss sliding easily in interdental spaces and special teeth-cleaning tools is important even when the gingiva is inflamed and bleeding. The regular use of alcohol-free mouthwash protecting from gingivitis is the last step in eliminating oral pathogens and the oral care routine during pregnancy. Additionally, it is crucial to emphasise the need to replace regularly the toothbrush. An interesting research on oral dysbiosis suggested that the use of probiotics and paraprobiotics can reduce oral pathogenic bacteria load significantly [97].

Beside the adequate oral care, the healthy diet is also of importance, as it may have an impact on the correct periodontal status, as well. A 2022 study reports of the significance of the intake of nutrients rich in fiber, vitamins (most of all, vitamin C) and minerals, preferring unsaturated fatty acids as opposed to saturated ones in relation to the periodontal status. The authors concluded that the Mediterranean diet has a beneficial impact on alleviating gingivitis [98].

Apart from the obstetrician-gynecologist, the health visitor has an important role in educating the patients. We think that there is considerable space for improvement in this respect in Hungary. The health visitor is supposed to supply the availability of the assigned regional dental practice and to allay the patient's fears and misbeliefs according to which treatment during pregnancy may be adverse to the fetus [93]. The health visitor is a widely known and respected person, especially in smaller towns and villages, their opinion is of particular importance among pregnant women, so the trust invested in their and their direct influence could indeed increase the willingness to attend the dental screening. Since there is no organised dental screening and treatment after completing secondary school studies in Hungary, the health education of adults should be more accentuated.

It is imperative to raise the attention of women of fertile age that periodontal diseases are supposed to be treated before the planned pregnancy and the mothers-to-be would start one of the most significant periods of their life having obtained adequate education in oral hygiene. We can assert that dental screenings and treatment deserve a prominent place besides sufficient information and education in pregnancy care, as these can be instrumental in preventing premature births. Premature births put pressure on the individual, the family, the society, and the healthcare system from ethical, health-related, and economic perspectives.

By adopting a prevention-orientated approach, the mums-to-be can promote their own and the fetus' health and the prolongation of the pregnancy which would benefit from attending periodontal screening - or treatment if necessary - prior to conception, so that by ensuring sufficient oral health status they would support uncomplicated pregnancy outcomes from a dental health perspective.

## 9. Conclusions

I. In group G a significant positive correlation was found between the SBI and the GA of the patients at periodontal examination ( $r = 0.252$ ,  $p = 0.04$ ). The growth of the BOP frequency for in each study group was positively correlated with the GA at the periodontal examination.

II. The correlation was statistically significant in group P, in which a significantly lower newborn weight was observed with an increase in SBI. This means that a more severe periodontal disease was associated with a lower BW ( $r = -0.587$ ,  $p = 0.001$ ). We found a negative correlation between SBI and BW, regardless of the periodontal status, but this correlation didn't reach the level of significance statistically ( $r = -0.181$ ,  $p = 0.058$ ).

III. By our results, when the SBI was higher, a lower GA was recorded at the time of delivery, regardless of which study group the patient belonged to. Corroborating this observation, we found a negative correlation in the study group G. This meant that those patients with a higher SBI gave birth sooner, at a lower GA. However, our observations cannot be claimed to be statistically significant, as the results are just below the necessary level ( $r = -0.233$ ,  $p = 0.057$ ).

IV. According to the results of our research, the poor maternal periodontal status (i.e. the presence of periodontal diseases) can negatively affect the obstetrical outcome by reducing the neonatal birth weight.

V. In our research it is worthy of note that the number of healthy patients amongst those taking part in the survey was substantially low (15.3% of the total patients), and this can be an important message related to the role of pre-conceptional periodontal care for women who want to have a pregnancy in the near future.

VI. It can be seen how important the education on the adequate oral hygiene and the periodontal screening of mothers-to-be are, also how the periodontal health programs assimilated into prenatal care and the cooperation between the obstetrician and the dentist could prove to be crucial in preventing pregnancy complications, e.g. low BW or preterm birth.

VII. Apart from the correct daily oral care routine, attending periodontal examinations - or treatments, if necessary - before and during pregnancy could significantly contribute to an obstetric outcome uncomplicated from the periodontal perspective.

VIII. Our research confirms the existence of certain connections between periodontal diseases and obstetrical outcomes highlighted by several other research, however, various studies were unable to find significant correlations, so we ourselves see the need and potential gain in conducting further research into the field.

## 10. Acknowledgements

I am indebted to **Gábor Németh**, Professor and Head of the Department of Obstetrics and Gynecology, University of Szeged for providing the conditions and for his encouraging attitude to make my research work possible.

I would like to express my honest thank to my thesis supervisor, **Tibor Novák** M.D., Ph.D., Med. Habil., Deputy Head of the Department of Obstetrics and Gynecology, University of Szeged for his guidance.

I would like to express my sincere gratitude to **Márta Radnai**, Professor of the Department of Prosthodontics, University of Szeged for her kind help, invaluable advices and instructions.

I wish to express my special gratitude to my family.

I am very thankful for my husband, **Zoltán** and my son, **Benedek** for giving me a peaceful and supportive background.

I would also like to acknowledge my parents' - **Edit and László** - contribution in being a true inspiration both in my scientific work and my life.

## 11. References

1. Battancs E., G.I., Pál A., Novák T., Eller J., L. Kókai E., Radnai M. , *Terhes nők szájhygiénes ismeretei, szokásai az ezredfordulón Délkelet-Magyarországon*. Fogorv Szle, 2011: p. 75-79.
2. Sebestyén A, B.I., Dózsa Cs, Pál M, Bánóczy J. , *Fogászati preventív vizsgálatok Magyarországon*. IME, 2003: p. 15-22.
3. Offenbacher, S., et al., *Periodontal infection as a possible risk factor for preterm low birth weight*. J Periodontol, 1996. **67**(10 Suppl): p. 1103-13.
4. Turner, M. and S.R. Aziz, *Management of the pregnant oral and maxillofacial surgery patient*. J Oral Maxillofac Surg, 2002. **60**(12): p. 1479-88.
5. Ismail, S.K. and L. Kenny, *Review on hyperemesis gravidarum*. Best Pract Res Clin Gastroenterol, 2007. **21**(5): p. 755-69.
6. Doucedé, G., et al., *[Tooth and pregnancy, a public health issue]*. Presse Med, 2019. **48**(10): p. 1043-1050.
7. Orosz M, S.B., Gábris K., *A terhességi epulis klinikai és patológiai jellemzői* Fogorv SZzle, 2007(100): p. 233-236.
8. Sooriyamoorthy, M. and D.B. Gower, *Hormonal influences on gingival tissue: relationship to periodontal disease*. J Clin Periodontol, 1989. **16**(4): p. 201-8.
9. Lindhe, J. and P.I. Branemark, *Changes in vascular permeability after local application of sex hormones*. J Periodontal Res, 1967. **2**(4): p. 259-65.
10. Yenen, Z. and T. Atacag, *Oral care in pregnancy*. J Turk Ger Gynecol Assoc, 2019. **20**(4): p. 264-268.
11. Abraham-Inpijn, L., O.V. Polsacheva, and J.E. Raber-Durlacher, *[The significance of endocrine factors and microorganisms in the development of gingivitis in pregnant women]*. Stomatologia (Mosk), 1996. **75**(3): p. 15-8.
12. Steinberg, B.J., et al., *Oral health and dental care during pregnancy*. Dent Clin North Am, 2013. **57**(2): p. 195-210.
13. Carrillo-de-Albornoz, A., et al., *Gingival changes during pregnancy: III. Impact of clinical, microbiological, immunological and socio-demographic factors on gingival inflammation*. J Clin Periodontol, 2012. **39**(3): p. 272-83.
14. Offenbacher, S., et al., *Effects of periodontal therapy during pregnancy on periodontal status, biologic parameters, and pregnancy outcomes: a pilot study*. J Periodontol, 2006. **77**(12): p. 2011-24.
15. Belcher, C., M. Doherty, and S.P. Crouch, *Synovial fluid neutrophil function in RA: the effect of pregnancy associated proteins*. Ann Rheum Dis, 2002. **61**(4): p. 379-80.
16. *WHO: recommended definitions, terminology and format for statistical tables related to the perinatal period and use of a new certificate for cause of perinatal deaths. Modifications recommended by FIGO as amended October 14, 1976*. Acta Obstet Gynecol Scand, 1977. **56**(3): p. 247-53.
17. Daskalakis, G., et al., *Preterm Labor: Up to Date*. Biomed Res Int, 2019. **2019**: p. 4870938.
18. McCormick, M.C., *The contribution of low birth weight to infant mortality and childhood morbidity*. N Engl J Med, 1985. **312**(2): p. 82-90.
19. Liu, L., et al., *Global, regional, and national causes of under-5 mortality in 2000-15: an updated systematic analysis with implications for the Sustainable Development Goals*. Lancet, 2016. **388**(10063): p. 3027-3035.
20. Goldenberg, R.L. and D.J. Rouse, *Prevention of premature birth*. N Engl J Med, 1998. **339**(5): p. 313-20.

21. Beck, S., et al., *The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity*. Bull World Health Organ, 2010. **88**(1): p. 31-8.
22. Perin, J., et al., *Global, regional, and national causes of under-5 mortality in 2000-19: an updated systematic analysis with implications for the Sustainable Development Goals*. Lancet Child Adolesc Health, 2022. **6**(2): p. 106-115.
23. KSH, *Koraszülöttek és kis súlyú újszülöttek Magyarországon*. <https://www.ksh.hu/docs/hun/xftp/idoszaki/pdf/koraszull16.pdf>, 2017.
24. KSH, *Statikszikai tükök - Csecsemőhalálozás*. <https://www.ksh.hu/docs/hun/xftp/stattukor/csecsemohalalozas.pdf>, 2019.
25. *European Perinatal Health Report, Europe 2015-2019*. [https://www.europeristat.com/images/Euro-Peristat\\_Fact\\_sheets\\_2022\\_for\\_upload.pdf](https://www.europeristat.com/images/Euro-Peristat_Fact_sheets_2022_for_upload.pdf), 2022.
26. Luu, T.M., et al., *Preterm birth: risk factor for early-onset chronic diseases*. CMAJ, 2016. **188**(10): p. 736-746.
27. Ream, M.A. and L. Lehwald, *Neurologic Consequences of Preterm Birth*. Curr Neurol Neurosci Rep, 2018. **18**(8): p. 48.
28. Z., P., *Perinatológia Kézikönyve*. Medicina Könyvkiadó Zrt. Budapest, 2016.
29. Goldenberg, R.L., et al., *Medical, psychosocial, and behavioral risk factors do not explain the increased risk for low birth weight among black women*. Am J Obstet Gynecol, 1996. **175**(5): p. 1317-24.
30. KSH, *A nők átlagos életkora gyermekük születésekor*. [https://www.ksh.gov.hu/docs/hun/eurostat\\_tablak/tab1/tps00017.html](https://www.ksh.gov.hu/docs/hun/eurostat_tablak/tab1/tps00017.html).
31. Mantel, A., A.L. Hirschberg, and O. Stephansson, *Association of Maternal Eating Disorders With Pregnancy and Neonatal Outcomes*. JAMA Psychiatry, 2020. **77**(3): p. 285-293.
32. Hendler, I., et al., *The Preterm Prediction Study: association between maternal body mass index and spontaneous and indicated preterm birth*. Am J Obstet Gynecol, 2005. **192**(3): p. 882-6.
33. Goldenberg, R.L., et al., *Epidemiology and causes of preterm birth*. Lancet, 2008. **371**(9606): p. 75-84.
34. Pearlstein, T., *Use of psychotropic medication during pregnancy and the postpartum period*. Womens Health (Lond), 2013. **9**(6): p. 605-15.
35. O'Halloran, K. and J.T. Spickett, *The interaction of lead exposure and pregnancy*. Asia Pac J Public Health, 1992. **6**(2): p. 35-9.
36. Signorello, L.B., et al., *Female survivors of childhood cancer: preterm birth and low birth weight among their children*. J Natl Cancer Inst, 2006. **98**(20): p. 1453-61.
37. Goldenberg, R.L., et al., *Sexually transmitted diseases and adverse outcomes of pregnancy*. Clin Perinatol, 1997. **24**(1): p. 23-41.
38. McDonald, H.M., et al., *Vaginal infection and preterm labour*. Br J Obstet Gynaecol, 1991. **98**(5): p. 427-35.
39. Rohlffing, A.B., et al., *Maternal cardiovascular disease risk factors as predictors of preterm birth in California: a case-control study*. BMJ Open, 2020. **10**(6): p. e034145.
40. Sarkar, M., et al., *Non-alcoholic fatty liver disease in pregnancy is associated with adverse maternal and perinatal outcomes*. J Hepatol, 2020. **73**(3): p. 516-522.
41. Hladunewich, M.A., *Chronic Kidney Disease and Pregnancy*. Semin Nephrol, 2017. **37**(4): p. 337-346.
42. Petri, M., *Pregnancy and Systemic Lupus Erythematosus*. Best Pract Res Clin Obstet Gynaecol, 2020. **64**: p. 24-30.
43. Beharee, N., et al., *Diagnosis and treatment of cervical cancer in pregnant women*. Cancer Med, 2019. **8**(12): p. 5425-5430.



44. Mannisto, T., et al., *Maternal psychiatric disorders and risk of preterm birth*. Ann Epidemiol, 2016. **26**(1): p. 14-20.
45. Goldenberg, R.L., J.C. Hauth, and W.W. Andrews, *Intrauterine infection and preterm delivery*. N Engl J Med, 2000. **342**(20): p. 1500-7.
46. Cassell, G.H., et al., *Isolation of Mycoplasma hominis and Ureaplasma urealyticum from amniotic fluid at 16-20 weeks of gestation: potential effect on outcome of pregnancy*. Sex Transm Dis, 1983. **10**(4 Suppl): p. 294-302.
47. Agrawal, V. and E. Hirsch, *Intrauterine infection and preterm labor*. Semin Fetal Neonatal Med, 2012. **17**(1): p. 12-9.
48. Mercer, B.M., et al., *The preterm prediction study: effect of gestational age and cause of preterm birth on subsequent obstetric outcome*. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Am J Obstet Gynecol, 1999. **181**(5 Pt 1): p. 1216-21.
49. Smith, G.C., J.P. Pell, and R. Dobbie, *Interpregnancy interval and risk of preterm birth and neonatal death: retrospective cohort study*. BMJ, 2003. **327**(7410): p. 313.
50. Jakobsson, M., et al., *Preterm delivery after surgical treatment for cervical intraepithelial neoplasia*. Obstet Gynecol, 2007. **109**(2 Pt 1): p. 309-13.
51. Yu, H.F., et al., *Association between polycystic ovary syndrome and the risk of pregnancy complications: A PRISMA-compliant systematic review and meta-analysis*. Medicine (Baltimore), 2016. **95**(51): p. e4863.
52. Krupa, F.G., et al., *Predictors of preterm birth*. Int J Gynaecol Obstet, 2006. **94**(1): p. 5-11.
53. Dunietz, G.L., et al., *Assisted reproduction and risk of preterm birth in singletons by infertility diagnoses and treatment modalities: a population-based study*. J Assist Reprod Genet, 2017. **34**(11): p. 1529-1535.
54. Murray, S.R. and J.E. Norman, *Multiple pregnancies following assisted reproductive technologies--a happy consequence or double trouble?* Semin Fetal Neonatal Med, 2014. **19**(4): p. 222-7.
55. Excellence, N.I.f.H.a.C., *Preterm labour and birth, Quality standard* <https://www.nice.org.uk/guidance/qs135>, 2016.
56. Gibbs, R.S., et al., *A review of premature birth and subclinical infection*. Am J Obstet Gynecol, 1992. **166**(5): p. 1515-28.
57. Romero, R., et al., *Infection in the pathogenesis of preterm labor*. Semin Perinatol, 1988. **12**(4): p. 262-79.
58. Hillier, S.L., et al., *A case-control study of chorioamnionic infection and histologic chorioamnionitis in prematurity*. N Engl J Med, 1988. **319**(15): p. 972-8.
59. Offenbacher, S., *Periodontal diseases: pathogenesis*. Ann Periodontol, 1996. **1**(1): p. 821-78.
60. Novak, T., et al., *Prevention of preterm delivery with periodontal treatment*. Fetal Diagn Ther, 2009. **25**(2): p. 230-3.
61. Novak, T., et al., *Could Poor Periodontal Status be a Warning Sign for Worse Pregnancy Outcome?* Oral Health Prev Dent, 2020. **18**(1): p. 165-170.
62. Collins, J.G., et al., *Effects of a Porphyromonas gingivalis infection on inflammatory mediator response and pregnancy outcome in hamsters*. Infect Immun, 1994. **62**(10): p. 4356-61.
63. Bi, W.G., et al., *Effect of periodontal treatment in pregnancy on perinatal outcomes: a systematic review and meta-analysis*. J Matern Fetal Neonatal Med, 2021. **34**(19): p. 3259-3268.
64. Mitchell-Lewis, D., et al., *Periodontal infections and pre-term birth: early findings from a cohort of young minority women in New York*. Eur J Oral Sci, 2001. **109**(1): p. 34-9.

65. Lopez, N.J., P.C. Smith, and J. Gutierrez, *Periodontal therapy may reduce the risk of preterm low birth weight in women with periodontal disease: a randomized controlled trial.* J Periodontol, 2002. **73**(8): p. 911-24.
66. Xiong, X., et al., *Periodontal disease and adverse pregnancy outcomes: a systematic review.* BJOG, 2006. **113**(2): p. 135-43.
67. Michalowicz, B.S., et al., *Treatment of periodontal disease and the risk of preterm birth.* N Engl J Med, 2006. **355**(18): p. 1885-94.
68. Vergnes, J.N. and M. Sixou, *Preterm low birth weight and maternal periodontal status: a meta-analysis.* Am J Obstet Gynecol, 2007. **196**(2): p. 135 e1-7.
69. Radnai, M., et al., *Benefits of periodontal therapy when preterm birth threatens.* J Dent Res, 2009. **88**(3): p. 280-4.
70. Sanz, M., K. Kornman, and E.F.P.A.A.P.w. working group 3 of the joint, *Periodontitis and adverse pregnancy outcomes: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases.* J Periodontol, 2013. **84**(4 Suppl): p. S164-9.
71. *Expanded Human Oral Microbiom Database V3.1.* <https://www.homd.org/>, 2023.
72. Sanz, M., et al., *Role of microbial biofilms in the maintenance of oral health and in the development of dental caries and periodontal diseases. Consensus report of group 1 of the Joint EFP/ORCA workshop on the boundaries between caries and periodontal disease.* J Clin Periodontol, 2017. **44 Suppl 18**: p. S5-S11.
73. Hajishengallis, G. and R.J. Lamont, *Beyond the red complex and into more complexity: the polymicrobial synergy and dysbiosis (PSD) model of periodontal disease etiology.* Mol Oral Microbiol, 2012. **27**(6): p. 409-19.
74. Kononen, E., et al., *Population-based study of salivary carriage of periodontal pathogens in adults.* J Clin Microbiol, 2007. **45**(8): p. 2446-51.
75. Stingu, C.S., et al., *Microbial profile of patients with periodontitis compared with healthy subjects.* Quintessence Int, 2012. **43**(2): p. e23-31.
76. Sconyers, J.R., J.J. Crawford, and J.D. Moriarty, *Relationship of bacteremia to toothbrushing in patients with periodontitis.* J Am Dent Assoc, 1973. **87**(3): p. 616-22.
77. Loe, H. and J. Silness, *Periodontal Disease in Pregnancy. I. Prevalence and Severity.* Acta Odontol Scand, 1963. **21**: p. 533-51.
78. Raber-Durlacher, J.E., et al., *Experimental gingivitis during pregnancy and post-partum: clinical, endocrinological, and microbiological aspects.* J Clin Periodontol, 1994. **21**(8): p. 549-58.
79. Offenbacher, S., et al., *Potential pathogenic mechanisms of periodontitis associated pregnancy complications.* Ann Periodontol, 1998. **3**(1): p. 233-50.
80. *Dental plaque revisited--oral biofilms in health and disease.* J Ir Dent Assoc, 2000. **46**(3): p. 105.
81. Offenbacher, S., et al., *Role of periodontitis in systemic health: spontaneous preterm birth.* J Dent Educ, 1998. **62**(10): p. 852-8.
82. Madianos, P.N., et al., *Maternal periodontitis and prematurity. Part II: Maternal infection and fetal exposure.* Ann Periodontol, 2001. **6**(1): p. 175-82.
83. Gauthier, S., et al., *The origin of Fusobacterium nucleatum involved in intra-amniotic infection and preterm birth.* J Matern Fetal Neonatal Med, 2011. **24**(11): p. 1329-32.
84. Hujoel, P.P., et al., *The dentogingival epithelial surface area revisited.* J Periodontal Res, 2001. **36**(1): p. 48-55.
85. Gera, I., *Periodontal disease as a risk factor for systemic diseases.* Parodontális Medicina Semmelweis Kiadó, 2009: p. 203-215.
86. Park, C.W., et al., *An elevated maternal serum C-reactive protein in the context of intra-amniotic inflammation is an indicator that the development of amnionitis, an intense*

- fetal and AF inflammatory response are likely in patients with preterm labor: clinical implications.* J Matern Fetal Neonatal Med, 2013. **26**(9): p. 847-53.
87. Sargent, I.L., A.M. Borzychowski, and C.W. Redman, *Immunoregulation in normal pregnancy and pre-eclampsia: an overview.* Reprod Biomed Online, 2007. **14 Spec No 1**: p. 111-7.
  88. Tettamanti, L., et al., *Pregnancy and periodontal disease: does exist a two-way relationship?* Oral Implantol (Rome), 2017. **10**(2): p. 112-118.
  89. Parczen Orsolya, P.L., Bogdanov Anita, Virok Dezső, *A fogágybetegség és a patológiás terhesség kapcsolata.* Magyar Nőorvosok lapja, 2021: p. 75-84.
  90. Gürsoy M, G.F., *Biological mechanisms between periodontal diseases and pregnancy complications: a systematic review and meta-analysis of epidemiological association between adverse pregnancy outcomes and periodontitis - an update of the review by Ide & Papapanou.*  
<https://www.efp.org/fileadmin/uploads/efp/Documents/Campaigns/OralHealthandPregnancy/Reports/review-biological-mechanisms-corr-4.0.pdf>, 2013.
  91. Mahapatra, A., et al., *Maternal periodontal status, oral inflammatory load, and systemic inflammation are associated with low infant birth weight.* J Periodontol, 2021. **92**(8): p. 1107-1116.
  92. Takeuchi, N., et al., *Relationship between periodontal inflammation and fetal growth in pregnant women: a cross-sectional study.* Arch Gynecol Obstet, 2013. **287**(5): p. 951-7.
  93. Ressler-Maerlender, J., R. Krishna, and V. Robison, *Oral health during pregnancy: current research.* J Womens Health (Larchmt), 2005. **14**(10): p. 880-2.
  94. Moore, P.A., *Selecting drugs for the pregnant dental patient.* J Am Dent Assoc, 1998. **129**(9): p. 1281-6.
  95. Hwang, S.S., et al., *The association between maternal oral health experiences and risk of preterm birth in 10 states, Pregnancy Risk Assessment Monitoring System, 2004-2006.* Matern Child Health J, 2012. **16**(8): p. 1688-95.
  96. Gera, I., *A várandós nő parodontális egészségi állapota és a terhességi komplikációk közötti kapcsolat* Orvosi Hetilap 2018: p. 999–1007
  97. Scribante, A., A. Butera, and M. Alovise, *Customized Minimally Invasive Protocols for the Clinical and Microbiological Management of the Oral Microbiota.* Microorganisms, 2022. **10**(4).
  98. Bartha, V., et al., *How to Measure Adherence to a Mediterranean Diet in Dental Studies: Is a Short Adherence Screener Enough? A Comparative Analysis.* Nutrients, 2022. **14**(6).

## 12. Scientific publications related to the subject of the thesis and appendices

**I.**

Article

# Maternal Periodontal Status as a Factor Influencing Obstetrical Outcomes

Petra Völgyesi <sup>1</sup>, Márta Radnai <sup>2</sup>, Gábor Németh <sup>1</sup>, Krisztina Boda <sup>3</sup>, Elena Bernad <sup>4,5,6,\*</sup> and Tibor Novák <sup>1</sup>

<sup>1</sup> Department of Obstetrics and Gynecology, Faculty of Medicine, University of Szeged, 6725 109 Szeged, Hungary

<sup>2</sup> Department of Prosthodontics, Faculty of Medicine, University of Szeged, 6725 109 Szeged, Hungary

<sup>3</sup> Department of Medical Physics and Informatics, Faculty of Medicine, University of Szeged, 6725 109 Szeged, Hungary

<sup>4</sup> Department of Obstetrics and Gynecology, Faculty of Medicine, “Victor Babes” University of Medicine and Pharmacy, 300041 Timisoara, Romania

<sup>5</sup> Clinic of Obstetrics and Gynecology, “Pius Brinzeu” County Clinical Emergency Hospital, 300723 Timisoara, Romania

<sup>6</sup> Center for Laparoscopy, Laparoscopic Surgery and In Vitro Fertilization, “Victor Babes” University of Medicine and Pharmacy, 300041 Timisoara, Romania

\* Correspondence: bernad.elena@umft.ro

**Abstract:** *Background and Objectives:* Preterm birth as a complex phenomenon is influenced by numerous endogenic and exogenic factors, although its exact cause often remains obscure. According to epidemiological studies, maternal periodontal diseases, in addition to affecting general health, can also cause adverse pregnancy outcomes. Nonetheless, the existing results in the literature regarding this topic remain controversial. Consequently, our study aimed to determine the connection between poor maternal periodontal status and neonatal birth weight. *Materials and Methods:* A total of 111 primigravida–primiparous pregnant, healthy women underwent a periodontal examination in the second trimester of their pregnancies. Probing depth (PD) and bleeding on probing (BOP) were determined, and based on these diagnostic measurements, the patients were divided into three subgroups according to their dental status: healthy (H,  $n = 17$ ), gingivitis (G,  $n = 67$ ), and periodontitis (P,  $n = 27$ ). *Results:* Considering that poor maternal oral status is an influencing factor for obstetrical outcomes, the presence of PD and BOP (characterized by the sulcus bleeding index, SBI) was evaluated. In the case of P, defined as  $PD \geq 4$  mm in at least one site and  $BOP \geq 50\%$  of the teeth, a significant correlation between BOP and a low neonatal birth weight at delivery ( $p = 0.001$ ) was found. An analysis of the relationship between SBI and gestational age (GA) at the time of the periodontal examination in the different dental status groups showed a significant correlation between these parameters in the G group ( $p = 0.04$ ). *Conclusion:* Our results suggest that a worse periodontal status during pregnancy may negatively affect obstetrical outcomes, especially the prematurity rate and newborn weight. Therefore, the importance of periodontal screening to prevent these complications is undeniable.

**Keywords:** preterm birth; gingivitis; periodontitis; neonatal birth weight

**Citation:** Völgyesi, P.; Radnai, M.; Németh, G.; Boda, K.; Bernad, E.; Novák, T. Maternal Periodontal Status as a Factor Influencing Obstetrical Outcomes. *Medicina* **2023**, *59*, 621. <https://doi.org/10.3390/medicina59030621>

Academic Editors: Dimitrios Papandreou and Benito Chiofalo

Received: 12 January 2023

Revised: 9 March 2023

Accepted: 16 March 2023

Published: 20 March 2023



**Copyright:** © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

## 1. Introduction

Prematurity is a global health issue that is becoming the leading cause of newborn morbidity and mortality worldwide [1]. According to the latest data from the World Health Organization (WHO), approximately 15 million preterm births (PBs) occur worldwide each year [2]. Over the years, many risk factors have been identified that may be associated with preterm birth and low birth weight, including age, tobacco use, alcohol use, and infections [3]. In 1996, Offenbacher et al. were the first to report a possible correlation between periodontal disease and preterm birth [4], and, since then, an increasing

number of studies have addressed the relationship between the two conditions [5,6]. Periodontal diseases include gingivitis and periodontitis, mainly caused by inappropriate oral hygiene or dental plaque misalignment [7].

Gingivitis, a milder and reversible pathological condition, manifests itself as inflammation of the gums due to accumulated bacterial plaque. When chronic inflammation extends from superficial to deep tissues, severe damage occurs in the tooth-supporting apparatus, which can lead to periodontitis. Initially, the clinical signs of these periodontal ailments include gingival edema and bleeding, and in the case of insufficient oral hygiene and/or regular dental care, with the deterioration of this condition and the development of periodontal pockets, tooth loss can occur [8]. Interestingly, studies have shown that pregnancy-induced hormonal changes can further aggravate gingival inflammation or the severity of pre-existing periodontal diseases [9,10]. The elevated levels of progesterone and estrogen may increase vascular permeability, making fibrous tissues more vulnerable to bacteria and resulting in adverse gingival changes [11]. With this damaging phenomenon, oral pathogens (e.g., Gram-negative microorganisms) and their bacterial products can easily reach the uterus through the bloodstream, and, at the same time, microbial components and inflammatory mediators derived from periodontal disease can also circulate to the liver, where they can initiate an entire inflammatory cascade. Consequently, prostaglandin production increases, which may cause preterm uterine activity, premature rupture of membranes, cervical insufficiency, and preterm labor [12]. Scientific data have proven that preterm delivery is strongly associated not only with a higher level of gingival prostaglandin E2 but also with increased neonatal immunoglobulin M seropositivity for several oral bacteria.

In recent studies [13], the role and the clinical and microbiological management of the oral microbiota have been described, focusing on the personalization of periodontal clinical practices and a proactive approach.

Primarily, the most reliable diagnostic tools for the identification and classification of periodontal diseases are probing depth (PD) and bleeding on probing (BOP), characterized by the sulcus bleeding index (SBI) [14]. The present study aimed to evaluate the correlation between periodontal status, based on a clinical examination of PD and BOP, and obstetrical outcomes, including neonatal birth weight (BW) and gestational age (GA) at delivery.

## 2. Materials and Methods

### 2.1. Study Design

This prospective clinical study was conducted at the University of Szeged, Department of Obstetrics and Gynecology, where, based on the authors' previously published results, a dental unit was installed and where the examination of the selected pregnant patients was carried out. It is important to know that, in Hungary, all pregnancies that finish with deliveries are recorded in the national health system database. Dental examinations are compulsory during pregnancy, and this fact is noted in the Health Booklet, which follows an expectant woman from the start to the end of her pregnancy. A total of 111 healthy, without significant illnesses, primigravida–primiparous pregnant women were involved in this study, which was ethically approved by the Human Investigation Review Board of the Albert Szent-Györgyi Clinical Center, Szeged, Hungary, approval number (123/2019-SZTE). Patients were selected during regular pregnancy-related ultrasound examinations, performed around the gestational ages of 11 and 19 weeks. Multiple gestations or cases with any associated diseases or regular medications were excluded. The study period for the periodontal examinations was between 1 August 2019 and 29 February 2020. Szeged is the county seat of Csongrád-Csanád County, with a population of about 159,000 inhabitants. The Department of Obstetrics and Gynecology, a part of Albert Szent-Györgyi Medical School, is a state-financed unit and the only place where childbirth (about 2500/year) takes place in this city. Only inhabitants of Szeged were selected

to take part in this study in order to eliminate problems related to the scheduling of periodontal examinations for pregnant patients from other places. The ultrasound examinations were performed by authorized doctors, based on a previous schedule, with the medical unit conducting about 20 similar examinations/day. This number also includes pregnant women from other cities and villages because the department is the regional tertiary medical unit for the southeastern part of Hungary, serving four counties (Csongrád-Csanád, Békés, Bács-Kiskun, and the southern part of Jász-Nagykun Szolnok), with a total population of about 1.6 million inhabitants. In the study period, there were a total of 2860 ultrasound examinations, of which 1144 were carried out on inhabitants of Szeged. Finally, of this number, 111 primigravida–primipara, healthy women were included in the project and selected for periodontal examinations. The health status of all 111 patients was monitored throughout their pregnancies; all women gave birth at our institution. The patients were fully informed about the aim of this study, and they took part voluntarily after signing a written consent form. A dental unit was installed at the Department of Obstetrics and Gynecology, based on the author's previous studies concerning the association between maternal dental modification and obstetric outcomes, and it was used for the dental examinations. It was equipped with good lighting and the possibility of patient positioning. Gestational age was determined by carrying out sonographic measurements of the embryos in the first trimester.

Periodontal examinations were performed after the ultrasound screening, based on a previous appointment, by an experienced dentist, according to the WHO guidelines. Patients' periodontal status was determined using PD and BOP. A disposable periodontal probe, which had a 0.5 mm diameter tip, was used for these measurements. PD was measured at 6 sites per tooth (the mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual, and distolingual sites), with the exception of the third molars, while BOP was recorded after 15 s on a Yes/No scale at the same sites as where PD was previously determined. The criteria used in each group were as follows: periodontally healthy patients had a sulcus depth between 1 and 3 mm with non-detectable gingival bleeding; patients with gingivitis had the same PD as healthy individuals, but they also had a BOP  $\geq 25\%$ ; and patients with periodontitis had a PD  $\geq 4$  mm in at least one site and a BOP  $\geq 50\%$  of the teeth. The determination of periodontitis was based on PD and BOP, the two most important periodontal parameters. The selection of these factors was based on our previous clinical studies in this field. PD  $\geq 4$  mm is regarded as a "critical probing depth", while smaller PD values are considered normal. BOP is a well-accepted sign of periodontal inflammation, and BOP and PD together are significant factors in the staging of periodontal disease [5,6,14]. After the deliveries, GA and neonatal birth weight (BW) were analyzed, and correlations regarding the patient's previous periodontal status were explored. During the examination carried out by the dentist, in all cases, the expectant women were instructed on correct oral hygiene procedures, including toothbrush and dental floss usage. The patients were classified into 3 categories based on the results of the aforementioned measurements: 17 healthy individuals (H), 67 patients with gingivitis (G), and 27 patients with periodontitis (P). The BOP was recorded and determined for each tooth. The percentage of BOP cases was calculated according to the total number of teeth of the patient, and this approach was named the sulcus bleeding index (SBI). For example, if the total number of teeth was 28, and BOP was found in 25 teeth, the SBI was 89.28%.

Delivery was considered at-term if it occurred after the completion of the 37th week. Before this gestational age ( $24^{+0}$ – $36^{+6}$  weeks), it was noted as a preterm delivery. A low BW was defined if the newborn weight was under the 5th percentile.

## 2.2. Statistical Analysis and Graph Editing

The recruited patients were divided into three groups according to their dental status. The samples were characterised as the mean and standard deviation (SD) of the data. The group means were compared by a one-way ANOVA, which can be considered a generalisation of the Student's two-sample *t*-test for more than two groups. The linear

relationship between the examined variables was also examined by the calculation of Pearson's correlation coefficient and the regression line. The significance of the correlation (its *p*-value) was also given. Statistical analyses were performed using SPSS version 26, and *p* < 0.05 was considered to be statistically significant. Graphs were edited in Microsoft Excel.

### 3. Results

The recruited patients were divided into three groups, namely, H, G, and P, according to the different dental statuses diagnosed during pregnancy. The low rate of cases with a healthy dental status at the time of the periodontal examination was remarkable, and this can be an important message related to the role of pre-conceptional periodontal care for women who want to have a pregnancy in the near future. All patients enrolled in this study gave birth to their newborns at the Department of Obstetrics and Gynecology, the University of Szeged.

#### 3.1. The Main Gestational Age at Dental Examination, Gestational and Maternal Age at Delivery and Birth Weight at Delivery

The main gestational age at the dental examination, the gestational and maternal ages at delivery, and the birth weight at delivery are presented in Table 1. As shown, the observed difference in the birth weights of the three examined groups was found to be statistically non-significant.

**Table 1.** Sample characteristics in different dental status groups. Results are shown as means ( $\pm$ SD).

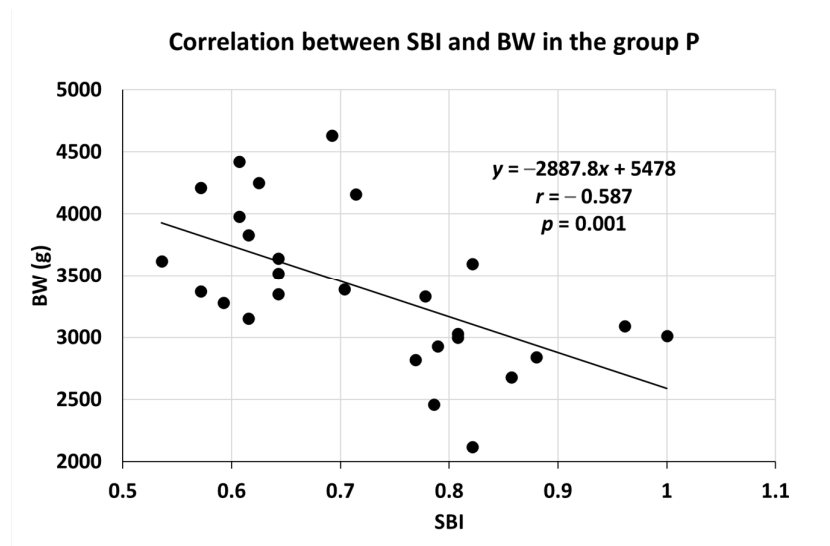
	Healthy (H) <i>n</i> = 17	Gingivitis (G) <i>n</i> = 67	Periodontitis (P) <i>n</i> = 27	ANOVA
Gestational age at dental examination (w)	16.24 $\pm$ 3.492	15.00 $\pm$ 3.516	14.00 $\pm$ 3.150	<i>p</i> = 0.111
Gestational age at delivery (w)	38.53 $\pm$ 1.772	39.07 $\pm$ 1.454	38.67 $\pm$ 1.414	<i>p</i> = 0.253
Maternal age at delivery (y)	31.25 $\pm$ 4.337	30.91 $\pm$ 5.197	29.53 $\pm$ 6.309	<i>p</i> = 0.464
Birth weight (g)	3518.82 $\pm$ 548.212	3402.24 $\pm$ 541.443	3396.67 $\pm$ 611.826	<i>p</i> = 0.726

Analysis of invariance: ANOVA

#### 3.2. Correlation between SBI and BW in Group P

After a further investigation of these data, it was clearly visible that the correlation was the most pronounced and statistically significant in the P group, in which a significantly lower newborn weight was observed with an increase in SBI. This means that a more severe periodontal disease was associated with a lower BW ( $r = -0.587$ , *p* = 0.001). The data are presented in Figure 1.

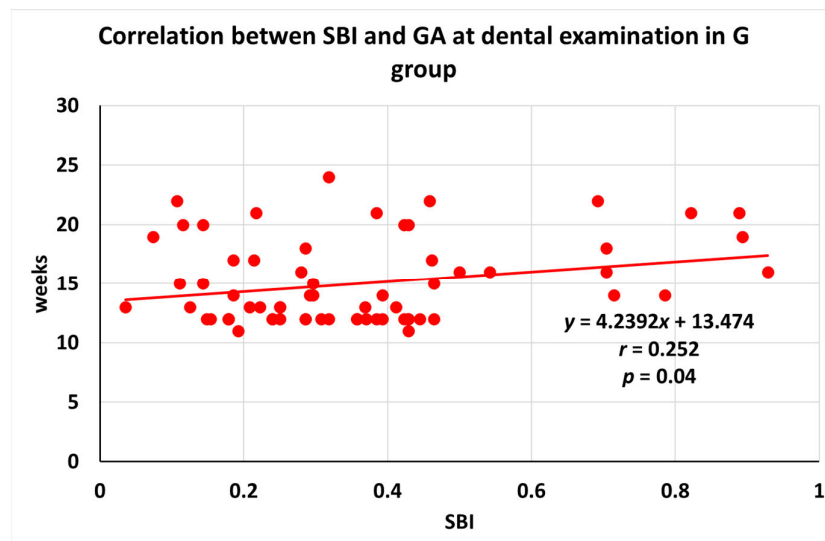




**Figure 1.** Correlation between SBI and BW in group P. Results are shown as means ( $\pm$ SD). BW = birth weight; SBI = sulcus bleeding index; P = periodontitis;  $n = 111$ ; and  $p < 0.05$  was considered statistically significant.

**3.3. Correlation between SBI and GA at Dental Examination in Different Dental Status Groups**

A detailed analysis showed a significant positive correlation ( $r = 0.252$ ,  $p = 0.04$ ) between SBI and patients' GA at the dental examination in the G group. These detailed data are presented in Figure 2 and Table 2, where the rate of G at the time of the dental examination can be seen. Being a significant linear correlation, Figure 2 gives a more detailed picture of this relationship.



**Figure 2.** Correlation between SBI and GA at dental examination in the G group. Results are shown as means ( $\pm$ SD). G = gingivitis; GA = gestational age; SBI = sulcus bleeding index;  $n = 111$ ; and  $p < 0.05$  was considered statistically significant.

**Table 2.** Correlation between SBI and GA at periodontal examination in different dental status groups;  $p < 0.05$  was considered statistically significant.

Group	N	Correlation Coefficient	$p$ Value
Healthy	17	$r = -0.391$	$p = 0.120$
Gingivitis	67	$r = 0.252$	$p = 0.04$
Periodontitis	27	$r = 0.127$	$p = 0.527$
Total	111	$r = -0.035$	$p = 0.714$

#### 4. Discussion

Dental hygiene is very important during pregnancy. Preventive or diagnostic dental treatment is highly recommended at any time throughout pregnancy, along with a proper oral hygiene routine every day. Although we did not observe a connection between poor dental status and premature delivery (Table 1), our results demonstrate a significant correlation between P and a low BW at delivery ( $p = 0.001$ ), meaning that pregnant women with a higher BOP (and, subsequently, a higher SBI) might have an increased risk of having lower BW newborns. These data are in line with the findings of Sanz et al., who previously revealed the role of hormonal and inflammatory processes in premature birth as a consequence of periodontal disease. Cytokine production and endotoxins released by oral microorganisms evoke the activation of the inflammatory cascade, which may contribute to the initiation of preterm parturition [15]. Preterm birth and a low BW may also carry a risk of predisposition to later neurological and motor impairments, together with malnutrition problems; thus, preventive medical interventions should be performed [16].

Moreover, in line with BW, gestational age at dental examination was also correlated with BOP. Interestingly, G was found to be higher at a significant rate at the time of the dental examinations ( $p = 0.04$ ). In the context of these results, we verified that BOP had a positive correlation with the patient's gestational age at the medical check-ups, drawing our attention to the importance of dental screening. Based on these results, it can be concluded that a worse periodontal status during pregnancy may negatively affect obstetrical outcomes. As a methodological limitation of this study, we note the relatively low number of cases. The most important cause of this was the beginning of the COVID-19 pandemic, which, at that moment, stopped study-related dental examinations. Moreover, this patient number limitation makes it impossible to differentiate between late prematurity ( $34^{+0}$ – $36^{+6}$  GW), prematurity ( $28^{+0}$ – $33^{+6}$  GW), and extreme prematurity ( $24^{+0}$ – $27^{+6}$  GW) and examine their correlations with maternal dental status. Still, regarding these causes, the results of our study have a powerful message, illustrating the importance of oral health during pregnancy.

Similar to our findings, Cho et al. found that pregnant women with dental caries participated in screenings less frequently [17]; however, clinical trials support the fact that preventive dental care can play a major role in the improvement of birth outcomes [18]. Both quantitative and qualitative studies regarding this issue have corroborated that women may have fears of dental examinations during pregnancy [19]. Although a high proportion of pregnant women experience dental problems (e.g., gingival bleeding, dental caries, and tooth mobility), only 30–40% seek medical advice during pregnancy. There may be many factors behind this pattern, but most of the time, it is due to a previous negative experience or a lack of education regarding oral hygiene. Since there is a strong correlation between poor dental status and pregnancy outcomes, raising awareness of oral health is indispensable [20]. Preventive dental and periodontal care, especially before and, if necessary, during pregnancy, is fundamental to maintaining both mothers' and newborns' health, and, for this exact reason, effective collaboration between obstetricians and dentists is essential [21,22]. Oral health promotion and education about proper dental care in pregnancy are indispensable for the prevention of pregnancy-associated complications, such as prematurity and neonatal low BW.

However, Scribante et al. [13] focused on the role of the balance of oral dysbiosis. They stated that using probiotics and paraprobiotics can lead to a statistically significant reduction in oral pathogenic bacterial load.

## 5. Conclusions

Periodontal diseases, such as gingivitis and periodontitis, mainly occur due to inappropriate oral hygiene. Pregnancy-induced hormonal changes further aggravate pre-existing periodontal diseases and can ultimately lead to adverse pregnancy outcomes. Our results indicate that there is a connection between periodontal status during pregnancy and obstetrical outcomes. We, therefore, believe that periodontal health programs linked to maternity are crucial for the prevention and diagnosis of periodontal diseases in pregnant women. By means of oral health education, a higher proportion of pregnancy and birth-related complications could be prevented.

Based on the obtained results, we can consider that poor maternal oral status is an influencing factor for worse obstetrical outcomes. In particular, the dental modifications associated with hemorrhage of the gingiva and periodontal pockets are involved. These modifications are detectable as early as the first trimester, and they can influence obstetrical outcomes, resulting, for example, in a lower newborn weight.

**Author Contributions:** Conceptualization, T.N.; methodology, P.V. and M.R.; formal analysis, K.B.; investigation, P.V. and M.R.; resources, G.N.; data curation, T.N. and K.B.; writing—original draft preparation, P.V.; writing—review and editing, T.N.; visualization, K.B. and E.B.; supervision, G.N. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** This study was ethically approved by the Human Investigation Review Board of the Albert Szent-Györgyi Clinical Center, Szeged, Hungary, approval number (123/2019-SZTE), approval date was 30/05/2019.

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in this study.

**Data Availability Statement:** All data used to support the findings of this study are included within the article.

**Conflicts of Interest:** The authors declare no conflicts of interest.

## References

1. Daskalakis, G.; Arabin, B.; Antsaklis, A. CaberoRoura, Preterm Labor: Up to Date. *Biomed. Res. Int.* **2019**, *2019*, 4870938.
2. Liu, L.; Oza, S.; Hogan, D.; Chu, Y.; Perin, J.; Zhu, J.; Lawn, J.; Cousens, S.; Mathers, C.; Black, R. Global, regional, and national causes of under-5 mortality in 2000–15: An updated systematic analysis with implications for the Sustainable Development Goals. *Lancet* **2016**, *388*, 3027–3035.
3. Beck, S.; Wojdyla, D.; Say, L.; Betran, A.; Merialdi, M.; Requejo, J.; Rubens, C.; Menon, R.; Van Look, P. The worldwide incidence of preterm birth: A systematic review of maternal mortality and morbidity. *Bull. World Health Organ.* **2010**, *88*, 31–38.
4. Offenbacher, S.; Katz, V.; Fertik, G.; Collins, J.; Boyd, D.; Maynor, G.; McKaig, R.; Beck, J. Periodontal Infection as a Possible Risk Factor for Preterm Low Birth Weight. *J. Periodontol.* **1996**, *67* (Suppl. 10S), 1103–1113.
5. Novak, T.; Radnai, M.; Gorzo, I.; Urban, E.; Orvos, H.; Eller, J.; Pal, A. Prevention of preterm delivery with periodontal treatment. *Fetal Diagn. Ther.* **2009**, *25*, 230–233.
6. Novak, T.; Nemeth, G.; Kozinszky, Z.; Urban, E.; Gorzo, I.; Radnai, M. Could Poor Periodontal Status be a Warning Sign for Worse Pregnancy Outcome? *Oral Health Prev. Dent.* **2020**, *18*, 165–170.
7. Kinane, D.; Stathopoulou, P.; Papapanou, P. Periodontal diseases. *Nat. Rev. Dis. Prim.* **2017**, *3*, 17038.
8. Pihlstrom, B.; Michalowicz, B.; Johnson, N. Periodontal diseases. *Lancet* **2005**, *366*, 1809–1020.
9. Carrillo-de-Albornoz, A.; Figuero, E.; Herrera, D.; Cuesta, P.; Bascones-Martinez, A. Gingival changes during pregnancy: III. Impact of clinical, microbiological, immunological and socio-demographic factors on gingival inflammation. *J. Clin. Periodontol.* **2012**, *39*, 272–283.
10. Offenbacher, S.; Lin, D.; Strauss, R.; McKaig, R.; Irving, J.; Barros, S.; Moss, K.; Barrow, D.; Hefti, A.; Beck, J.D. Effects of periodontal therapy during pregnancy on periodontal status, biologic parameters, and pregnancy outcomes: A pilot study. *J. Periodontol.* **2006**, *77*, 2011–2024.
11. Yenen, Z.; Atacag, T. Oral care in pregnancy. *J. Turk. Ger. Gynecol. Assoc.* **2019**, *20*, 264–268.

12. Takeuchi, N.; Ekuni, D.; Irie, K.; Furuta, M.; Tomofuji, T.; Morita, M.; Watanabe, T. Relationship between periodontal inflammation and fetal growth in pregnant women: A cross-sectional study. *Arch. Gynecol. Obstet.* **2013**, *287*, 951–957.
13. Scribante, A.; Butera, A.; Alovise, M. Customized minimally invasive protocols for the clinical and microbiological management of the oral microbiota. *Microorganisms* **2022**, *10*, 675. <https://doi.org/10.3390/microorganisms10040675>.
14. Radnai, M.; Pal, A.; Novak, T.; Urban, E.; Eller, J.; Gorzo, I. Benefits of periodontal therapy when preterm birth threatens. *J. Dent. Res.* **2009**, *88*, 280–284.
15. Sanz, M.; Kornman, K.; Working Group 3 of the Joint EFP/AAP Workshop. Periodontitis and adverse pregnancy outcomes: Consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. *J. Periodontol.* **2013**, *84* (Suppl. 4), S164–S169.
16. Ream, M.; Lehwald, L. Neurologic Consequences of Preterm Birth. *Curr. Neurol. Neurosci. Rep.* **2018**, *18*, 48.
17. Cho, G.; Kim, S.; Lee, H.; Kim, H.; Lee, K.; Han, S.; Oh, M. Association between dental caries and adverse pregnancy outcomes. *Sci. Rep.* **2020**, *10*, 5309.
18. Hwang, S.; Smith, V.; McCormick, M.; Barfield, W. The association between maternal oral health experiences and risk of preterm birth in 10 states, Pregnancy Risk Assessment Monitoring System, 2004–2006. *Matern. Child Health J.* **2012**, *16*, 1688–1695.
19. Ressler-Maerlender, J.; Krishna, R.; Robison, V. Oral health during pregnancy: Current research. *J. Women's Health* **2005**, *14*, 880–882.
20. AlRatroot, S.; Alotaibi, G.; Albishi, F.; Khan, S.; Nazir, M.A. Dental Anxiety Amongst Pregnant Women: Relationship With Dental Attendance and Sociodemographic Factors. *Int. Dent. J.* **2022**, *72*, 179–185.
21. Terzic, M.; Aimagambetova, G.; Terzic, S.; Radunovic, M.; Bapayeva, G.; Lagana, A. Periodontal Pathogens and Preterm Birth: Current Knowledge and Further Interventions. *Pathogens* **2021**, *10*, 730.
22. Mainas, G.; Ide, M.; Rizzo, M.; Magan-Fernandez, A.; Mesa, F.; Nibali, L. Managing the Systemic Impact of Periodontitis. *Medicina* **2022**, *58*, 621.

**Disclaimer/Publisher's Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

**II.**

# A fogászati szűrővizsgálatok jelentősége a terhesgondozásban



Völgyesi Petra dr.<sup>1</sup>, Radnai Márta dr.<sup>2</sup>, Németh Gábor dr.<sup>1</sup>,  
Boda Krisztina dr.<sup>3</sup>, Novák Tibor Antal dr.<sup>1</sup>

<sup>1</sup>SZTE, Szent-Györgyi Albert Klinikai Központ, Szülészeti és Nőgyógyászati Klinika, Szeged  
(Igazgató: Prof. dr. Németh Gábor)

<sup>2</sup>SZTE, Fogorvostudományi Kar Fogpótlástani Tanszék, Szeged (Tanszékvezető és dékán: Prof. dr. Baráth Zoltán)

<sup>3</sup>SZTE, Szent-Györgyi Albert Orvostudományi Kar és SZTE Természettudományi és Informatikai Kar,  
Orvosi Fizikai és Orvosi Informatikai Intézet, Szeged (Igazgató: Prof. dr. Peták Ferenc)

**Célkitűzés:** Tanulmányunkban arra szeretnénk volna választ kapni, hogy van-e összefüggés a terhesek parodontális vizsgálatkor jegyzett terhességi kora és a vizsgálat során észlelt szondázási vérzések gyakorisága között, és ennek milyen kapcsolata van a szüléskori terhességi kora, valamint az újszülöttkori testsúlyal.

**Anyag és módszer:** Az SZTE Szülészeti és Nőgyógyászati Klinikáján együttműködve az SZTE Fogorvostudományi Kar Fogpótlástani Tanszékével 2019. augusztus 1. és 2020. február 29. között 1144 szegedi lakcímmel rendelkező terhes ultrahangvizsgálatát végeztük el. Közülük 111 alapbetegséggel nem rendelkező, primigravida-primipara szegedi lakos került beálgatásra, majd részesült parodontális vizsgálatban. A páciensek második trimeszterbeli parodontális vizsgálatát követően a terhességeket szülésig nyomon követve elemeztük a születéskori terhességi kort és az újszülöttek születési súlyát.

**Eredmények:** Tanulmányunkban pozitív összefüggést találtunk a fogászati vizsgálatkor észlelt magasabb terhességi kor és a nagyobb ínyvérzési index között. Negatív összefüggést tapasztaltunk (bár a szignifikancia szintjét éppen nem érték el) a parodontális vizsgálatkor észlelt ínyvérzési index növekedése és a szüléskori terhességi kor, valamint az újszülött születési súlya között.

**Következtetések:** Jelen tanulmányunk is megerősíti a preconceptionális és terhesség alatti fogászati szűrővizsgálatok jelentőségét, beleértve a betegedukációt is.

*Kulcsszavak: gingivitis, parodontitis, szondázási mélység, szondázási vérzés, ínyvérzési index*

## The significance of dental screening in pregnancy care

**Objective:** The aim of our study was to examine the existence of a possible connection between the gestational age at periodontal screening and the sulcus bleeding index. We also wanted to examine the relationship of sulcus bleeding index with gestational age at delivery and neonatal birth weight.

**Materials and methods:** Our study was collaboration between the Obstetrics and Gynecology Department, Faculty of Medicine, and the Department of Prosthodontics, Faculty of Dentistry, University of Szeged. A total of 111 healthy, primigravida-primiparous pregnant, citizens of Szeged were involved between the 1<sup>st</sup> of August 2019 and the 29<sup>th</sup> of February 2020, selected from the 1144 gravidas who had applied. After the periodontal examination in the second trimester, we followed our patients until their delivery, analysing the gestational age and neonatal birth weight.

**Results:** We found a positive connection between the higher gestational age at the time of periodontal examination and the higher sulcus bleeding index. We found a negative correlation (which did not reach the level of significance) between the higher sulcus bleeding index and the gestational age at delivery, and also between the higher sulcus bleeding index and the newborns' birth weight.

**Conclusion:** Our results confirm the importance of dental screening in the pre-conceptional period and during pregnancy and patient education as well.

*Keywords: gingivitis, periodontitis, probing depth, bleeding on probing, sulcus bleeding index*

**Rövidítésjegyzék:** ANOVA (Analysis of variance): varianciaelemzés; BOP (bleeding on probing): szondázási vérzés; CRP: C-reaktív protein; IL-1 $\alpha$ : Interleukin-1 alfa; IL-6: Interleukin-6; PD (probing depth): szondázási mélység; PGE2: Prostaglandin E2; SBI (sulcus bleeding index): ínyvérzési index; SPSS (Statistical Package for Social Sciences): statisztikai megoldásokat szolgáltató programcsomag; WHO (World Health Organization): Egyészségügyi Világszervezet

Érkezett: 2023. április 3. Közlésre elfogadva: 2023. május 2. Received: 3 April 2023. Accepted: 2 May 2023

Levelezési cím: Dr. Völgyesi Petra, SZTE Szent-Györgyi Albert Klinikai Központ, Szülészeti és Nőgyógyászati Klinika, 6725 Szeged, Semmelweis u.1. E-mail: med.volgyesipetra@gmail.com

## Bevezetés

Bár Magyarországon a terhesség alatti fogászati ellenőrzés a terhesgondozásban részesülő gravidáknak térítésmentes, a páciensek csak nagyon alacsony arányban veszik ezt igénybe [1]. Ez az arány országos átlagban 2001-ben 15,5% volt, ami napjainkra javult valamelyest, de még egyetemi nagyvárosban sem tapasztaltak 30%-ot meghaladó arányt [2]. Hazai felmérések szerint a terhesek körében kevéssé ismert a várandósság alatti fogászati ellenőrzések, kezelések lehetősége, annak jelentősége. Az utóbbi években a terhesség alatti fogágybetegségek és a szülészeti kimenetel kapcsolatát számos kutatócsoport vizsgálta. Ezen vizsgálatok gyakori végpontja a parodontális státusz és a koraszülés vizsgálata, annak minden anyai és magzati szövődményével [3]. Egy várandós nő szájhigiénéjére számos tényező hat: megváltozott étkezési szokások (terhességi hányás okozta pH-eltolódás, következményes szájszárazság vagy épp gyakori evés miatt romló szájhigiénia), valamint a terhességi hormonális változások. Mindezek befolyásolják a szájüregi nyálkahártya, a fogágy és a fogazat állapotát. Várandósság alatt a nyál összetétele, a szájüregi normálfloora megváltozik, fokozódik a nyálkiválasztás (főként az első trimeszterben), ugyanakkor a nyálsemelegesítő, antibakteriális hatása csökken. Terhességben nőhet a dentális plakk mennyisége, fokozódik a terhességi ínygyulladásra való hajlam [4]. A terhesség hormonális változásai miatt a fogíny és fogágy szöveteinek kapilláris-permeabilitása megnő [5], a baktériumok könnyebb bejutásával a tasakfal szöveteibe, ugyanakkor fokozódik az íny ödémára, vérzékenységre való hajlama, ezt súlyosbíthatja a nem megfelelő szájhigiéné. Terhességben tehát ugyanazon baktériumszám mellett könnyebben alakulhat ki gingivitis, fogínyvérzés. Mivel az íny érzékenysége terhességben a megfelelő tisztítás mértékének csökkenésével jár együtt, ez fokozza a fogszuvasodás kockázatát is. A vörös, ödémás, vérzékeny íny a terhesség akár teljes ideje alatt jelentkezhet, ám a gingivitis a második és harmadik trimeszterben a leggyakoribb. A gingivitis egy viszonylag enyhe, könnyen kezelhető, reverzibilis állapot, amelyet az íny területén felhalmozódott bakteriális plakk okoz. A kialakuló baktériumréteg irritálja az ínyt, és annak ödémájához, gyulladásához vezet. Vérzéssel járhat, amelyet leggyakrabban fogmosás, fogselymezés közben vagy keményebb táplálékra (pl. almára) való harapás során tapasztal a páciens. A fogak mellett (parodontális) tasakok jönnek létre a fogíny és a fogak között, amelyek a gyulladásos folyamat krónikus-sá válásával, valamint a megfelelő parodontális kezelés hiányában egyre mélyebbek lesznek, meggyengítve a fogak támasztószövetét. Ez az állapot gyulladásához, parodontitishez vezethet. Ennek előrehaladtával felmerülhet a fogíny visszahúzódásának, csontpusztulásnak, esetleges csontvesztésnek a veszélye. Korábbi tanulmányok ismertették a fogágybetegségek számos negatív hatását a szülészeti kimenetelre, ami a szüléskori terhességi kort és az újszülöttkori testsúlyt illeti, valamint megerősítést nyert az összefüggés is, hogy a terhesség alatti parodontális kezelés csökkenti a perinatális mortalitást és a koraszülés kockázatát, valamint javítja az újszülöttek súlyát [6].

Galloway volt az első (1931), aki felvetette, hogy a parodontium Gram-negatív anaerob baktériumok általi fertőzése káros hatással lehet a terhes nőre és a fejlődő magzatra. Majd Offenbacher és munkatársai (1996) tanulmányukban ismét ráirányították a figyelmet a fogászati kórképek szülészeti kimenetelre gyakorolt hatásainak jelentőségére, a parodontális státusz és a koraszülés közötti összefüggésre [3]. Ezt követően egyre több hasonló témájú közlemény látott napvilágot. Azóta új megvilágításba került az ínyvérzés mértékének, a szondázási mélység, a szájüregi inflammatorikus folyamatok (utóbbi bakteriológiai és molekuláris szintű) vizsgálata, hiszen összefüggést véltek felfedezni a terhes méhre gyakorolt hatásaikon keresztül a koraszülés gyakoriságára. E kapcsolat feltárására számos állatkísérlet, epidemiológiai vizsgálat, szisztémás elemzés és metaanalízis került publikálásra [3, 6].

A szájüregben mára bizonyítottan 700-800 mikrobiális species található, túlnyomó részük a normálfloát alkotó ártalmatlan, kommenzális mikroorganizmus (Gram-pozitív orális baktériumok, köztük *Actinomyces*- és *Streptococcus*-törzsek). Mellettük a patogén mikrobák alapvetően kis számban vannak jelen [7]. A normálfloora arányainak patogén baktériumok irányába történő eltolódása (diszbakteriózis) már jelentős szervezetet károsító, domináns immunválaszt kiváltó bakteriális mikroflóra megjelenéséhez vezet [8]. A fogágybetegségek hátterében ezen mikrobák tagjai közül leggyakrabban az obligát vagy fakultatív anaerob Gram-negatívok állnak, mint az *Aggregatibacter actinomycetemcomitans*, *Fusobacterium nucleatum*, *Porphyromonas gingivalis*, *Tannerella forsythia*, *Treponema denticola*, *Prevotella intermedia*, *Filifactor alocis* és *Campylobacter rectus* [9, 10]. Egészséges egyénben a szájüregi patogén törzsek aránya alacsony vagy az immunrendszer még erős negatív hatásokat is képes semlegesíteni. Amennyiben a szervezet és a bakteriális mikroflóra egyensúlya felborul, az önmagában lehetővé teszi a fogágybetegség, parodontitis kialakulását. A felszín nagysága, amin keresztül a baktériumok a szövetekbe jutnak nagy jelentőséggel bír. A bakterémia ugyan rövid ideig tart (15-30 perc), esetenként azonban minden fogmosáskor, keményebb étel rágásakor ismétlődik, akár több évtizeden keresztül.

A parodontitis Gram-negatív baktériumok által kiváltott gyulladásos megbetegedés, amely érinti a fogágyat: az ínyt és a fogakat tartó csontállományt. Ez állandó, krónikus gyulladást jelent, amely során a parodontális tasak a Gram-negatív baktériumok „raktárának” tekinthető.

Direkt mechanizmus által a parodontopatogén baktériumok a fogágybetegség miatt fellazult mélyebb szövetekből, parodontális tasakokból hematogén disszemináció révén eljutnak a feto-placentaris szövetekhez és az amnionfolyadékba, ahol másodlagos fertőzést, lokális immunválaszt és gyulladást (chorioamnionitis) hoznak létre [11]. Egészséges parodontiumú egyének esetében a dentogingivális felszín kb. 5 cm<sup>2</sup>, azonban parodontitis esetében ez akár 8-20 cm<sup>2</sup>-re nőhet [12]. Generalizált idült parodontitisben a fogak mentén 4-5 mm-es mélységű tasakokkal, a tasakok falának sérült hámrétegeből összeadódva közel tenyérnyi nyitott sebfelszínen át többek közt az obli-

gát anaerob, endotoxint termelő bakteriális kolónia állandó kapcsolatban áll a szervezettel [13]. Az indirekt mechanizmus lényege, hogy a krónikusan gyulladt parodontiumból gyulladáshoz vezető mediátorok (intermedierek, citokinek) jutnak a szisztémás keringésbe és ezek közvetlenül és/vagy a gravida májában akutfázis-reakciót indukálva, akutfázis-fehérjék (C-reaktív protein, CRP) és fibrinogén expresszáldása révén okoznak másodlagos gyulladást a feto-placentaris egységben [14]. Mind a lokális immunválasz következtében kialakuló chorioamnionitis, mind a gyulladáshoz vezető mediátorok, amelyek haematogén disszemináció révén érik el a foeto-placentaris egységet, hatást gyakorolnak annak metabolizmusára [15]. A keringő mikrobák toxinjai és toxikus metabolitjaik direkt szöveti toxicitást okoznak, illetve a chorion fiziológiás citokintermelésének (főként IL-1 $\alpha$ , IL-6 és TNF $\alpha$ ) és általa a prosztaglandin termelésének (PGE2) kóros indukciója korai méhtevékenységhez, a cervix megrövidüléséhez és dilatációjához, a magzatburok megrepedéséhez, így fenyegető koraszüléshez vagy koraszüléshez vezethet [16].

A terhesek kb. 41%-a számol be fogmosás közbeni fogínyvérzésről [1]. Ez a tény irányította figyelmünket erre a gyakori tünetre. A fogágybetegségek vizsgálatára és beosztására használatos diagnosztikus lehetőség a fognyak melletti szondázási mélység (probing depth, PD) vizsgálata, valamint a vizsgálat során tapasztalt esetleges szondázási ínyvérzés (bleeding on probing, BOP). Ha egy fognál vérzést tapasztalunk, annak meglétét az adott foghoz rendeljük. Az ínyvérzési index (sulcus bleeding index, SBI) egy hányados, ami kifejezi a szondázás során jelentkező ínyvérzést mutató BOP-fogak arányát az összes vizsgált foghoz viszonyítva. Korábbi vizsgálatunkban összefüggést találtunk a parodontális vizsgálaton megjelent terhesek ínyvérzési indexe és a fogászati vizsgálatkor megállapított terhességi kor között [17]. Jelen vizsgálatunkban célul tűztük ki ezen összefüggés pontosabb megismerését, valamint vizsgálatát a szüléskori terhességi kor esetén egyes fogágybetegségeknél.

## Anyag és módszer

Prospektív klinikai vizsgálatunkat a Szegedi Tudományegyetem Szülészeti és Nőgyógyászati Klinikáján végeztük 2019. augusztus 1. és 2020. február 29. között. A vizsgálati csoport tagjai az intézetünkben terhesgondozásban részesülő gravidák közül kerültek beválogatásra. A páciensek a terhességük 11. és 19. hete között szülészeti ultrahangvizsgálatban részesültek, és információt kaptak a vizsgálati részvétel lehetőségéről. A terhesgondozás során elvégzett fogászati szűrővizsgálat elvégzése ajánlott, ami a terhesgondozás során rögzítésre kerül. A terhesek minden esetben teljes körű felvilágosítást és a beleegyező nyilatkozat aláírását követően kerültek be a vizsgálatba. Többes terhesség, bármilyen alapbetegség megléte, illetve rendszeres gyógyszervesedés esetén a páciens kizárásra került. A terhesek nyomon követése szempontjából fontosnak ítéltük, hogy szegedi lakcímük legyen és klinikánkon tervezzék szülésüket. Ezen páciensek

terhességét, egészségi állapotuk alakulását így végig tudtuk követni egészen a szülésig. A hét hónap alatt 1144 szegedi lakcímmel rendelkező terhes ultrahangvizsgálatát végeztük el. Összesen 111 egészséges primigravida-primipara terhes felelt meg a követelményeknek, akiknek nem volt semmilyen ismert alapbetegsége. Vizsgálatunkat a Szent-Györgyi Albert Klinikai Központ Etikai Bizottságának engedélye alapján végeztük (123/2019-SZTE). A szerzők korábbi kutatásai kapcsán a klinika egyik helyiségében korábban már berendezésre került egy komplett fogászati vizsgálóállomás. A parodontális vizsgálatokat minden esetben fogszakorvos-kolléga végezte az Egészségügyi Világszervezet (World Health Organization, WHO) ajánlásai alapján. A vizsgálatok előtt szülészeti ultrahangvizsgálat történt, így a terhességi korok minden esetben rögzítésre kerültek. A fogászati felmérésünk során alapos parodontális vizsgálat történt, amely kiterjedt a plakk-akkumuláció, a szondázási mélység (PD) mérésére és az ennek kapcsán esetlegesen jelentkező szondázási vérzés (BOP) detektálására. A vizsgálat elvégzéséhez 0,5 mm átmérőjű parodontológiai szondát használtunk. A bölcsességfogak kivételével minden fog esetén, 6 helyen (mesiobuccalis, midbuccalis, distobuccalis, mesiolingualis, midlingualis, distolingualis) mértük meg a szondázási mélységet. A mérést követően 15 másodpercen belül, ha észleltünk vérzést, az adott foghoz rendeltük. A szondázási mélységet a marginális fogíny és a sulcus vagy a tasak legmélyebb pontja között jegyeztük. A pácienseket parodontális státuszuk alapján három csoportra osztottuk.

- Fogászati szempontból a páciens egészséges volt, ha a szondázási mélység 1-3 mm közé esett és nem tapasztaltunk vérzést.
- A fogíny gyulladása, gingivitis volt a diagnózis, ha hasonló szondázási mélység mellett a fogak legalább 25%-a mellett észleltünk vérzést.
- Parodontitis esetén a szondázási mélység legalább egy helyen elérte vagy meghaladta a 4 mm-t, és a fogak legalább 50%-a mellett azonosítottunk szondázási vérzést.

A szondázási mélység és a szondázásra jelentkező vérzés detektálásának jelentősége, valamint a szondázási mélység beosztása korábbi vizsgálataink eredményein alapul. Eddigi szakirodalmi ismereteink és tapasztalataink alapján a 4 mm-es szondázási mélység tekinthető parodontitis szempontjából kritikusnak. Mind a szondázási mélység, mind a szondázási vérzés megléte a nemzetközi irodalomban általánosan elfogadott jele a fogíny gyulladásának, a fogágybetegség állapotának felmérésére. Minden általunk vizsgált terhes szülése után a szüléskori terhességi kor és az újszülött születési súlya regisztrálásra került. Statisztikai számításaink során a folytonos változók átlagait a 3 csoportban egyszempontos ANOVA-val hasonlítottuk össze. Az ínyvérzési index kapcsolatát a terhességi korokkal és az újszülött születési súlyokkal lineáris korreláció-regresszió módszerrel elemeztük (Pearson's). Statisztikai számításainkhoz az SPSS software 26. verzióját használtuk, és a  $p < 0,05$  esetén mondtuk ki statisztikailag szignifikánsnak az eltérést.



## Eredmények

A pácienseinket parodontális státuszuk alapján Egészséges, Gingivitis és Parodontitis csoportokba osztottuk. 17 terhes bizonyult egészségesnek, 67 esetben találtuk a fogíny gyulladását, míg 27 páciens esetén parodontitis került megállapításra. A parodontális vizsgálat idején külön megvizsgáltuk az összes páciens esetén a terhességi kort (1. táblázat és 1. ábra).

Ennek figyelembevételével összesítettük a páciensek ínyvérzési indexét. Eredményeinket a 2. ábra tartalmazza. Azt találtuk, hogy a fogászati szempontból egészséges terhesekink alacsonyabb terhességi korban vettek részt parodontális vizsgálaton. Parodontitis esetén a vizsgálat időpontjában észlelt terhességi kor bár magasabb volt, de ez nem bizonyult szignifikánsnak.

Fogágybetegség megléte esetén (gingivitis: 67 páciens, parodontitis: 27 páciens), akiknek gyakrabban vérzett az ínyük, később mentek fogorvosi vizsgálatra. Ezt követően elemeztük a szülési adatokat. Megvizsgáltuk minden terhese-nél az ínyvérzési index összefüggését a szüléskori terhességi korról. Eredményeinket a 3. ábra foglalja össze.

Statisztikai elemzést végezve azt találtuk, hogy a gingivitis csoport eredményei a szignifikancia szintjét majdnem elérik (2. táblázat).

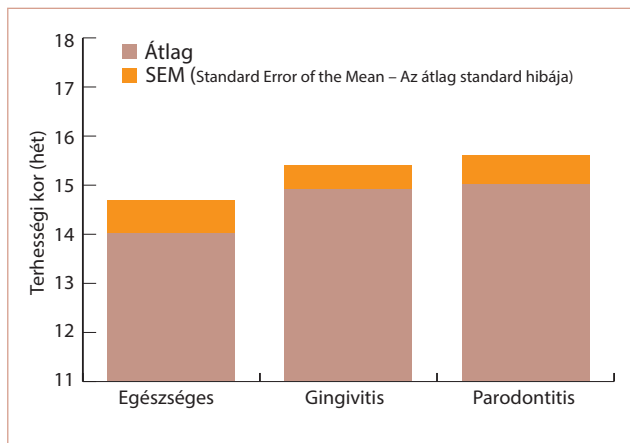
Bár itt gyengébb az összefüggés, a tendencia mindenesetre megfigyelhető, hogy ahogy az ínyvérzési index növekszik, úgy csökken a szüléskori terhességi kor (4. ábra).

1. táblázat: Terhességi kor a fogászati vizsgálatnál (hét) a parodontális státusz kategóriáiban

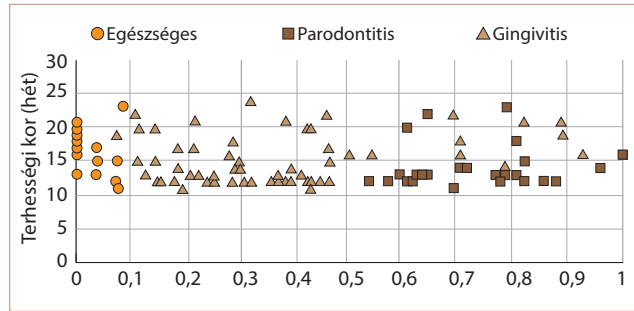
Fogászati kategóriák	N	Átlag (SEM)
Egészséges	17	14,00 (0,764)
Gingivitis	67	14,95 (0,423)
Parodontitis	27	15,00 (0,677)

ANOVA p = 0,111 SEM = standard error of the mean

A parodontális vizsgálat idején a terhességi korok rögzítésre kerültek. Figyelemre méltó a fogászati szempontból egészséges terhesek alacsony száma (15,3%).



1. ábra: Terhességi kor (hét) a parodontális vizsgálatnál  
A parodontális vizsgálat idején külön megvizsgáltuk az összes páciens esetén a terhességi kort.

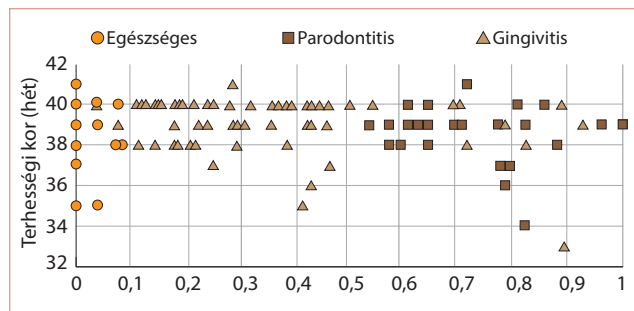


2. ábra: SBI és terhességi kor (hét) összefüggése a parodontális vizsgálatnál. Mind gingivitis mind parodontitis esetén a gravidák később mentek fogorvosi vizsgálatra.

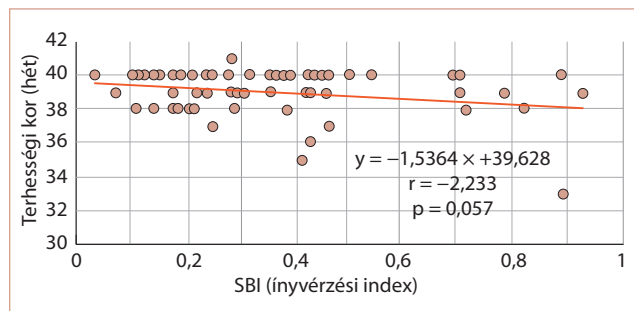
2. táblázat: Ínyvérzési index és a szüléskori terhességi kor a parodontális státusz kategóriáiban

Fogászati kategóriák	N	Korrelációs együttható (r)	p-érték (p)
Egészséges	17	-0,120	0,647
Gingivitis	67	-0,233	0,057
Parodontitis	27	-0,142	0,480
Összes	111	-0,120	0,21

A gingivitis csoport eredményei a szignifikancia szintjét majdnem elérik az ínyvérzési index és a szüléskori terhességi kor negatív összefüggésében.



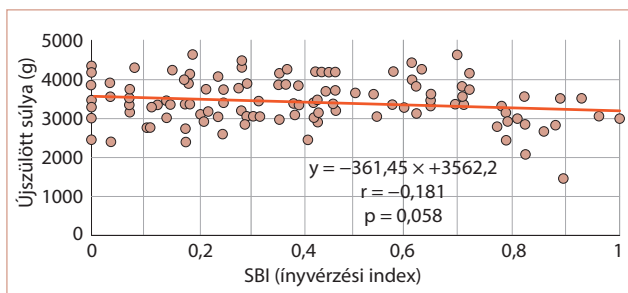
3. ábra: SBI és terhességi kor a születéskor (hét) összefüggése. Az ínyvérzési index növekedése esetén alacsonyabbnak bizonyult a szüléskori terhességi kor.



4. ábra: SBI és terhességi kor a születéskor (hét) összefüggése gingivitisben. A tendencia megfigyelhető, hogy ahogy nő az ínyvérzési index, úgy csökken a szüléskori terhességi kor.

Ezt követően megnéztük az ínyvérzési index és az újszülöttek születési súlya közötti összefüggést. A parodontális státuszról függetlenül vizsgálva enyhe negatív összefüggést kaptunk (5. ábra).

A korrelációs együttható  $r = -0,181$ ,  $p = 0,058$ , amely ugyan éppen nem szignifikáns 5% szinten, de azt majdnem eléri.



**5. ábra: SBI és újszülött súlya (g) közötti összefüggés**  
Az ínyvérzési index emelkedésével az újszülöttek súlya csökken.

Eredményünk a tendenciát mutatja, miszerint az ínyvérzési index emelkedésével az újszülöttek születési súlya csökken.

## Megbeszélés

Az irodalmi áttekintésből látható, hogy a koraszülések hátterében a szervezet egészét tekintve olyan fertőzések is állhatnak, amelyek kapcsolatáról korábban ismeretekkel nem rendelkezünk. Legtöbbször az urogenitális, a hüvelyi és nemi úton szerzett fertőzések szerepét vizsgálták a terhességi szövődmények kialakulásával kapcsolatba hozható infekciók közül, azonban azóta felmerült a terhes méhtől, mint célszervtől távolabb azonosítható fertőzésforrás jelentősége is, mint a különböző fogászati kórképek kialakulásáért felelős szájüregi gyulladással kapcsolatos folyamatok hátterében álló szubgingivális mikroorganizmusok. Az utóbbi időben egyre több vizsgálat kutatja a terhesség alatti szájhygiéné és a szülészeti kimenetel kapcsolatát [6, 16, 18, 19]. Egy 2021-es prospektív elemzés során vizsgálva az összefüggést az anyai parodontális állapot, a szájüregi gyulladással terhelés és a szérum C-reaktív protein (CRP) szintje, valamint a csecsemő születési súlya között, a szerzők arra a következtetésre jutottak, hogy a rossz anyai parodontális állapot, a megnövekedett szájüregi gyulladással terhelés és a fokozott szisztémás gyulladás káros hatással lehet a csecsemő születési súlyára [20].

Amint vizsgálatainkban is látszik, a terhesség során kialakult gingivitisz, esetleges parodontitisz rendelkező gravidák esetén csak megfelelő fogászati vizsgálat és kezelés esetén biztosítható a terhességet megelőző fogászati státusz. Mindezek fontosságát bizonyítják azok az adatok is, amelyek szerint ezen fogászati kórképek adekvát parodontológiai kezelése pozitív hatású a szülészeti kimenetelre [6]. Jelen kutatásunk eredményei a nemzetközi vizsgálatok adataihoz illeszkednek. A parodontális vizsgálatok során a szondázási mélység és a szondázásra megjelenő esetleges vérzéses válasz rögzítése megbízható vizsgálati módszer a fogágybetegségek felmérésére, és mint korábbi tanulmányokból ismert a szondázási ínyvérzés növekvő tendenciája összefüggésbe hozható a fenyegető koraszülés és a koraszülés kialakulásával [18]. Tanulmányunkban figyelemre méltó a fogászati szempontból egészséges terhesek alacsony száma (15,3%). Ez felhívja a figyelmet a prekoncepcionális szájhygiéné fontosságára. Bár a szülészeti protokollban szerepel a terhesek fogászati

szűrővizsgálata és kezelése, ennek ismerete a kismamák között mégis rendkívül alacsony. Sok páciens a fogmosáskor tapasztalt fogínyvérzésnek nem tulajdonít kellő jelentőséget. Nem tartják fontosnak és/vagy félnek a fogorvosi ellenőrzéstől, ezért nem vesznek részt az általuk vélhetően kellemetlennek minősített vizsgálaton [1]. Mint jelen tanulmányunkból látszik a panaszokkal rendelkező kismamák magasabb terhességi korban kerültek fogászati vizsgálatra. A fogmosáskor tapasztalt gyakoribb vérzés, rosszabb fogászati státusz magyarázhatja, hogy a páciensek egy része miért jelenik meg később fogászati vizsgálatokon. Korábbi kutatások bizonyították, hogy az egyének fogápolási szokásai, fogászati szűrővizsgálatokon való megjelenései földrajzi területenként komoly eltérést mutatnak [2]. Befolyásolja az iskolai végzettség [1], a gazdasági helyzet és számos egyéni tényező. Gyakran szembesülünk egyszerűen az információ hiányával.

Vizsgálatunk erősségének tekintjük, hogy minden bevont páciens esetén végzett részletes és alapos parodontológiai felmérést követően a gravidák terhességét egészen a szülésig végig követtük és pontos adatokkal rendelkezünk a szülészeti terhességi korról, valamint az újszülöttek testsúlyáról. Felmérésünk hiányossága azonban, hogy a COVID-19-pandémia kezdetével mind terheseinket, mind a fogászati ellátást végző személyzetet fokozott kockázatnak tettük volna ki, így a vizsgálatunk nem volt folytatható. Meglátásunk szerint nagyobb esetszám elérésével szignifikáns eredményeket tudtunk volna felmutatni az ínyvérzési index és a szülészeti terhességi kor, valamint az újszülöttek születési súlya összefüggésében. Mindezek miatt felmérésünk folytatását tervezzük. Irodalmi adatok alapján a választott vizsgálati fogászati módszerek adekvátak. Tapasztalataink szerint a pácienseink bevonásánál a tájékoztatás minden esetben sikeres volt, és a terhesek ezek ismeretében szívesen vállalták az extravizsgálatokat. Fontos észrevétel, hogy bár a parodontális vizsgálat alapossága miatt a páciensek részéről türelmes együttműködést igényelt, a visszajelzések alapján ezt senki nem találta kellemetlennek vagy elviselhetetlennek. Vizsgálatainkban a terhességi kor és a születési súly esetén a szignifikáns összefüggést nagyon megközelítettük, ám kimutatni nem tudtuk, amelyre befolyással lehet vizsgálatunk pandémia következtében alakult alacsony esetszáma. Számos közlemény született, amely a prekoncepcionális és a terhesség alatt fogászati vizsgálatok fontosságára hívja fel a figyelmet [16, 19, 21, 22].

Egyrészt a megfelelő oktatás és gondozás kiemelt jelentőségű, hiszen nem mindegy, hogy a fertilis kor kezdetén a páciens milyen fogászati státusszal bír. Nehezíti azonban a dolgunkat, hogy a magyar populációban alacsony a fogászati ellenőrzések rendszerességére való hajlandóság [1].

A helyes szájhygiénés gyakorlat elsajátítása elengedhetetlen, különös tekintettel az interdentális területek tisztítására. Ajánlott fogínygyulladás elleni fogkrém és a terhességben jellemző fokozott fogínyvérzési tendencia figyelembevételével finom vagy közepes sörteerősségű fejjel ellátott, lehetőleg elektromos fogkefe használata a hatékonyabb lepedékeltávolításra. A puha, fogközökben könnyen síkló fogszelvény és speciális fogtisztító eszközök használata akkor is fontos,

ha gingivitis esetén az íny gyulladt és vérzik. A fogínygyulladással szemben védelmet biztosító alkoholmentes szájvízzel történő rendszeres öblögetés a szájüregi kórokozók elpusztításának és a terhesség alatt végzett szájápolási rutin utolsó lépése. Mindezek mellett fontos kiemelni, hogy rendszeres időközönként a fogkefe cseréje szükséges.

A szájápolási szokások mellett nem szabad megfeledkezni az egészséges táplálkozás jelentőségéről, amely szintén hozzájárulhat a megfelelő parodontális státuszhoz. A rost- és vitamindús (elsősorban C-vitamin), ásványi anyagokban gazdag tápanyagok bevitelének, a telítetlen zsírsavak telítettekkel szemben történő preferálásának jelentőségéről számol be egy 2022-es tanulmány a parodontális státusz összefüggésében. A szerzők arra a következtetésre jutottak, hogy a mediterrán diéta kedvező hatással bír az ínygyulladás csökkentésére [23].

A szülés szakorvos mellett a védőnőnek is jelentős szerepe van a kellő információ átadásában. Azt gondoljuk, hogy Magyarországon ebben a tekintetben még nagyon sokat kellene fejlődnünk. A védőnő feladata adott esetben a területileg illetékes fogászati rendelés elérhetőségének biztosítása, a kismama félelmeinek és az általános tévhitek eloszlatása, amelyek szerint terhesség alatt a fogakat nem ajánlott kezelni. Főként kisebb településeken a védőnő személye sokak számára ismert, véleménye kiemelt jelentőséggel bír a várandósok körében, a belé vetett bizalom és az ő közvetlen ráhatása révén nagymértékben növelni lehet a hajlandóságot a fogászati szűrésen való megjelenésre. Tekintettel arra, hogy Magyarországon a középiskola elvégzése után nincs szervezett fogorvosi szűrés és kezelés, nagyobb hangsúlyt kell fektetni a felnőttek egészségnevelésére. Szükséges felhívni a fertilis korú nők figyelmét arra, hogy a fogágybetegséget célszerűbb lenne már a tervezett terhességek előtt kezelni, illetve a leendő édesanyák megfelelő felvilágosítást követően, szájápolási ismeretek birtokában kezdenék el életük egyik legjelentősebb időszakát.

Kijelenthetjük, hogy a terhesgondozásban megfelelő edukáció és tájékoztatás mellett méltó helyet kell biztosítanunk a fogászati szűrővizsgálatoknak és kezeléseknél, hiszen szerepük lehet a koraszülés megelőzésében. A koraszülés etikai, egészségügyi és gazdasági szinten is igen nagy terhet ró mind az egyénre, mind a családra, a társadalomra és az ellátórendszerre.

A profilaxisorientált szemlélet nélkülözhetetlen a leendő édesanyák és magzatuk egészségének megőrzése érdekében, ezért a szülészeti és fogászati együttműködés kiemelt fontosságú.

### Köszönetnyilvánítás

Kutatócsoportunk nevében szeretném köszönetemet kifejezni prof. dr. Radnai Mártának és prof. dr. Németh Gábornak, hogy vizsgálatainkhoz szükséges tárgyi és szakmai felteteleket biztosították.

### Érdeklődés, támogatások

A szerzőknek nincsenek érdeklődéseik.

### IRODALOM

- Battancs E, Gorzó I, Pál A, Novák T, Eller JL, Kókai E, Radnai M. Terhes nők szájhygiéne ismeretei, szokásai az ezredfordulón Délkelet-Magyarországon. *Fogorv Szle* 2011; 104(3): 75–79.
- Sebestyén A, Boncz I, Dózsa Cs, Pál M, Bánóczy J. Fogászati preventív vizsgálatok Magyarországon IME 2003; 2: 15–22.
- Offenbacher S, Katz V, Fertik G, Collins J, Boyd D, Maynor G, McKaig R, Beck J. Periodontal infection as a possible risk factor for preterm low birth weight. *J Periodontol* 1996; 67: 1103–1113.
- Orosz M, Szende B, Gábris K. A terhességi epulis klinikai és patológiai jellemzői. *Fogorv Szle* 2007; 100: 233–236.
- Sarrel M. The differential effects of oestrogens and progestins on vascular tone. *Human Reproduction Update* 1999; 5: 205–209.
- Bi WG, Emami E, Luo ZC, Santamaria C, Wei SQ. Effect of periodontal treatment in pregnancy on perinatal outcomes: a systematic review and meta-analysis. *J Matern Fetal Neonatal Med* 2019; 21: 1–10.
- Chen T, Yu W-H, Izard J, Baranova OV, Lakshmanan A, Dewhirst FE. The Human Oral Microbiome Database: a web accessible resource for investigating oral microbe taxonomic and genomic information. *Database J Biol Databases Curation* 2010; 2010. doi: 10.1093/database/baq013
- Hajishengallis G, Lamont RJ. Beyond the red complex and into more complexity: the polymicrobial synergy and dysbiosis (PSD) model of periodontal disease etiology. *Mol Oral Microbiol* 2012; 27: 409–419.
- Könönen E, Paju S, Pussinen PJ, et al. Population based study of salivary carriage of periodontal pathogens in adults. *J Clin Microbiol* 2007; 45: 2446–2451.
- Stingu CS, Jentsch H, Eick S, et al. Microbial profile of patients with periodontitis compared with healthy subjects. *Quintessence Int* 2012; 43: e23–e31.
- Gauthier S, Tétu A, Himaya E, et al. The origin of *Fusobacterium nucleatum* involved in intra-amniotic infection and preterm birth. *J Matern Fetal Neonatal Med* 2011; 24: 1329–1332.
- Hujoel PP, White BA, Garcia RI, Listgarten MA. The dentogingival epithelial surface area revisited. *J Periodont Res* 2001; 36: 48–55.
- Gera I, Gorzó I. Periodontal disease as a risk factor for systemic diseases. In: Gera I. (ed.) *Periodontology*. 2<sup>nd</sup> edn. A fogágybetegség mint az általános szervezeti betegségek rizikófaktora – Parodontális Medicina. In: Gera I. (szerk.) *Parodontológia*. 2. kiadás. Budapest: Semmelweis Kiadó; 2009. pp. 203–215.
- Park CW, Yoon BH, Park JS, et al. An elevated maternal serum C-reactive protein in the context of intra-amniotic inflammation is an indicator that the development of amnionitis, an intense fetal and AF inflammatory response are likely in patients with preterm labor: clinical implications. *J Matern Fetal Neonatal Med* 2013; 26: 847–853.
- Parczen O, Párducz L, Bogdanov A, Virok D. A fogágybetegség és a patológiás terhesség kapcsolata. *Magyar Nőorvosok Lapja* 2021; 84: 75–84.
- Gürsoy M, Graziani F. Biological mechanisms between periodontal diseases and pregnancy complications: a systematic review and meta-analysis of epidemiological association between adverse pregnancy outcomes and periodontitis – an update of the review by Ide & Papapanou (2013). *Oral Health and Pregnancy oralhealthandpregnancy.efp.org* 2018.
- Völgyesi P, Radnai M, Németh G, Boda K, Bernad E, Novák T. Maternal Periodontal Status as a Factor Influencing Obstetrical Outcomes. *Medicina (Open Access Journal by MDPI)* 2023; 59(3): 621 <https://doi.org/10.3390/medicina59030621>
- Novák T, Németh G, Kozinszky Z, Urbán E, Gorzó I, Radnai M. Could Poor Periodontal Status be a Warning Sign for Worse Pregnancy Outcome? *Oral Health Prev Dent* 2020; 18(1): 165–170. 6672.
- Perunovic ND, Rakic MM, Nikolic LI, et al. The association between periodontal inflammation and labor triggers (elevated cytokine levels) in preterm birth: a cross-sectional study. *J Periodontol* 2016; 87: 248–256.
- Mahapatra A, Nayak R, Satpathy A, Pati BK, Mohanty R, Mohanty G, Beura R. Maternal periodontal status, oral inflammatory load, and systemic inflammation are associated with low infant birth weight. *J Periodontol* 2021; 92(8): 1107–1116.
- Offenbacher S, Lieff S, Boggess KA, et al. Maternal periodontitis and prematurity. Part I: Maternal infections and fetal exposure. *Ann Periodontol* 2001; 6: 175–182.
- Offenbacher S, Jared HL, O'Reilly PG, et al. Potential pathogenic mechanisms of periodontitis-associated pregnancy complications. *Ann Periodontol* 1998b; 3: 233–250.
- Bartha V, Exner L, Meyer AL, Basrai M, Schweikert D, Adolph M, Bruckner T, Meller C, Woelber JP, Wolff D. How to Measure Adherence to a Mediterranean Diet in Dental Studies: Is a Short Adherence Screener Enough? A Comparative Analysis. *Nutrients* 2022; 14(6): 1300.

## **Appendices**

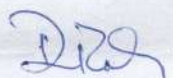
Co-author renoucement declarations

Appendix No 3.: Co-author renouncement declaration

**Co-author certification**

I, myself as a corresponding author of the following publication(s) declare that the authors have no conflict of interest, and Petra Völgyesi M.D., Ph.D. candidate had significant contribution to the jointly published research(es). Her duties included providing the patients with information, inviting and selecting patients, reviewing the relevant scientific literature and writing the article with her supervisor overseeing it. The results discussed in her thesis were not used and are not intended to be used in any other qualification process for obtaining her Ph.D. degree.

19.05.2023



date

author

The publication(s) relevant to the applicant's thesis:

1. Petra Völgyesi, Márta Radnai, Gábor Németh, Krisztina Boda, Elena Bernad, Tibor Novák. Maternal Periodontal Status as a Factor Influencing Obstetrical Outcomes. Medicina 2023, Volume 59, Issue 3, 621. **IF: 2,948**
2. Völgyesi Petra, Radnai Márta, Németh Gábor, Boda Krisztina, Novák Tibor. A fogászati szűrővizsgálatok jelentősége a terhesgondozásban. Magyar Nőorvosok Lapja 2023. **Under publishing**

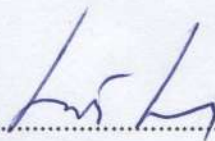
Appendix No 3.: Co-author renouncement declaration

**Co-author certification**

I, myself as a corresponding author of the following publication(s) declare that the authors have no conflict of interest, and Petra Völgyesi M.D., Ph.D. candidate had significant contribution to the jointly published research(es). Her duties included providing the patients with information, inviting and selecting patients, reviewing the relevant scientific literature and writing the article with her supervisor overseeing it. The results discussed in her thesis were not used and are not intended to be used in any other qualification process for obtaining her Ph.D. degree.

2023 05 19

date



author



The publication(s) relevant to the applicant's thesis:

1. Petra Völgyesi, Márta Radnai, Gábor Németh, Krisztina Boda, Elena Bernad, Tibor Novák. Maternal Periodontal Status as a Factor Influencing Obstetrical Outcomes. Medicina 2023, Volume 59, Issue 3, 621. **IF: 2,948**
2. Völgyesi Petra, Radnai Márta, Németh Gábor, Boda Krisztina, Novák Tibor. A fogászati szűrővizsgálatok jelentősége a terhesgondozásban. Magyar Nőorvosok Lapja 2023. **Under publishing**

Appendix No 3.: Co-author renouncement declaration

**Co-author certification**

I, myself as a corresponding author of the following publication(s) declare that the authors have no conflict of interest, and Petra Völgyesi M.D., Ph.D. candidate had significant contribution to the jointly published research(es). Her duties included providing the patients with information, inviting and selecting patients, reviewing the relevant scientific literature and writing the article with her supervisor overseeing it. The results discussed in her thesis were not used and are not intended to be used in any other qualification process for obtaining her Ph.D. degree.

19. May 2023

date

Dr Boda Krisztina

author

DR. BODA KRISZTINA

The publication(s) relevant to the applicant's thesis:

1. Petra Völgyesi, Márta Radnai, Gábor Németh, Krisztina Boda, Elena Bernad, Tibor Novák. Maternal Periodontal Status as a Factor Influencing Obstetrical Outcomes. Medicina 2023, Volume 59, Issue 3, 621. **IF: 2,948**
2. Völgyesi Petra, Radnai Márta, Németh Gábor, Boda Krisztina, Novák Tibor. A fogászati szűrővizsgálatok jelentősége a terhesgondozásban. Magyar Nőorvosok Lapja 2023. **Under publishing**

2023


Appendix No 3.: Co-author renouncement declaration

### Co-author certification

I, myself as a corresponding author of the following publication(s) declare that the authors have no conflict of interest, and Petra Völgyesi M.D., Ph.D. candidate had significant contribution to the jointly published research(es). Her duties included providing the patients with information, inviting and selecting patients, reviewing the relevant scientific literature and writing the article with her supervisor overseeing it. The results discussed in her thesis were not used and are not intended to be used in any other qualification process for obtaining her Ph.D. degree.

11.05.2023

date



author

The publication(s) relevant to the applicant's thesis:

1. Maternal Periodontal Status as a Factor Influencing Obstetrical Outcomes

Petra Völgyesi; Márta Radnai; Gábor Németh; Krisztina Boda; Elena Bernad; Tibor

Novák. Medicina 2023, Volume 59, Issue 3, 621. IF: 2,948



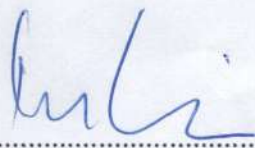
Appendix No 3.: Co-author renouncement declaration

**Co-author certification**

I, myself as a corresponding author of the following publication(s) declare that the authors have no conflict of interest, and Petra Völgyesi M.D., Ph.D. candidate had significant contribution to the jointly published research(es). Her duties included providing the patients with information, inviting and selecting patients, reviewing the relevant scientific literature and writing the article with her supervisor overseeing it. The results discussed in her thesis were not used and are not intended to be used in any other qualification process for obtaining her Ph.D. degree.

May 19, 2023

date



author

The publication(s) relevant to the applicant's thesis:

1. Petra Völgyesi, Márta Radnai, Gábor Németh, Krisztina Boda, Elena Bernad, Tibor Novák. Maternal Periodontal Status as a Factor Influencing Obstetrical Outcomes. Medicina 2023, Volume 59, Issue 3, 621. **IF: 2,948**
2. Völgyesi Petra, Radnai Márta, Németh Gábor, Boda Krisztina, Novák Tibor. A fogászati szűrővizsgálatok jelentősége a terhesgondozásban. Magyar Nőorvosok Lapja 2023. **Under publishing**