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

The significance of maternal periodontal status in prenatal care

Summary of the Ph.D. Thesis

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1. List of scientific publications related to the subject of this thesis

- 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.
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- Völgyesi Petra, Radnai Márta, Németh Gábor, Boda Krisztina, Novák Tibor. A fogászati szűrővizsgálatok jelentősége a terhesgondozásban. Magyar Nőorvosok Lapja 2023.

Under publishing

2. List of abbreviations

BOP	bleeding on probing
BW	birth weight
G	Gingivitis
GA	gestational age
Н	Healthy
IL	interleukin
Р	Periodontitis
PD	probing depth
PGE ₂	prostaglandin E ₂
r	correlation coefficient
SBI	sulcus bleeding index
TNF-α	tumor necrosis factor alpha

3. Introduction

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. 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 and low birth weight, including all respective maternal and fetal complications [3]. The pregnancy-induced hormonal changes may increase the risk of periodontal diseases (eg.

gingivitis or periodontitis) and exacerbate existing pathological conditions of the periodontium [4, 5]. Immunological changes during pregnancy also affect the oral health. The suppression of certain neutrophil functions may also explain the exacerbation of gingivitis [6]. Regarding the potential pathomechanism of the connection between periodontal diseases and preterm birth, two main paths have been identified in the last years. The periodontopathogenic bacteria reach the feto-placental 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 [7]. In the case of patients with healthy periodontium the periodontal sulcus area is approximately 5 cm^2 , however, with periodontitis, this surface can reach $8-20 \text{ cm}^2$ [8]. 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 [9]. 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 feto-placental 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) [10]. During pregnancy, the inflammatory response is strongly activated [11], attested by the increased expression of the inflammatory markers [12]. Both the chorioamnionitis arising from local immune response and the inflammatory mediators that reach the feto-placental unit via haematogenous dissemination have an impact on the metabolism of the feto-placental unit [13]. The proinflammatory cytokines, especially the interleukin (IL)-1, IL-6, tumor necrosis factor alpha (TNF- α) stimulate the prostaglandin E_2 (PGE₂) production by the placenta and chorioamnion. Prostaglandin assists the physiological regulation of the pregnancy, administering medicine containing prostaglandin leads to abortion or delivery [14]. The toxins of the circulating microbes, as

well as their toxic metabolites cause direct histological toxicity. The physiologic cytokine-production (especially the IL-1 α , IL-6 and TNF- α) of the chorion and through this the anomalous induction of PGE₂ can lead to early uterine activity, the shortening and dilatation of the cervix, the rupture of the amniotic membrane thus to threatening or actual preterm birth [15].

4. 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 gestational age (GA) at delivery and the neonatal birth weight (BW). We further investigated the possible connection between the GA at periodontal screening and the sulcus bleeding index (SBI), and its effect on the obstetrical outcome.

5. Material and methods

This prospective clinical study was conducted at the University of Szeged, Department of Obstetrics and Gynecology. 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. A dental unit had been installed at the department as part of the authors' previous research program and was used for this research, too. 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. The health status of all 111 patients was monitored throughout their pregnancies; all women gave birth at our institution. 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 (World Health Organization) 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 probing depth (PD), and the detection of bleeding on probing (BOP) possibly appearing as a result of probing. 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 (hereafter referred to as BOP tooth). 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 > 25% were identified as patients with gingivitis, and finally those patients with a $PD \ge 4$ 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 widely accepted as the most significant parameters to indicate periodontal inflammation, diagnose and state the severity of the periodontal diseases (staging) [16-18]. 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. The statistical samples were characterised as the mean and standard deviation (SD) of the data, where the group means were compared by a oneway 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 describing the significance of the correlation was also supplied. According to this, p < 0.05value 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).

6. Results

The 111 patients were classified into 3 categories based on the results of the measurements: 17 healthy individuals (H), 67 patients with gingivitis (G), and 27 patients with periodontitis (P). In group G a significant positive correlation was found between the SBI and the GA of the patients at periodontal examination, where r = 0.252 and p = 0.04. This means that in group G those patients who suffered from an increased SBI attended the periodontal examinations at a significantly higher GA. In the study groups the growth of the respective BOP frequency showed a positive correlation with the GA at the periodontal examination. Group H applied at the earliest GA for the periodontal examination, followed by the group G, then P. Patients in group P had the highest GA at the time of the periodontal examinations however, the correlation is statistically non-significant. 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). Irrespectively of the periodontal status we observed a negative correlation between the SBI and the BW that was just below the level of statistical significance (r = -0.181, p = 0.058). Independently of the study group status, the higher the SBI was, the lower GA at delivery was observed, too. We also found a negative correlation in group G in this regard. 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 (r = -0.233, p = 0.057). 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).

7. Discussion

Inappropriate oral hygiene is identified as the main contributing factor causing periodontal diseases such as gingivitis or periodontitis. 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 these periodontal diseases has a positive effect on the obstetrical outcome [19]. 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 adequate examination practices to diagnose periodontal diseases, 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 [16, 20]. 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 significant correlation between the poor dental status and premature delivery, however. 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 correlation between the SBI and GA at delivery in group G and the BW in all groups 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 can say that preventive oral care before and during the pregnancy is critical from both the mothers' and the newborns' perspective [21]. 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. 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 preventionorientated approach, the mums-to-be can promote their own and the fetus' health and the prolongation of the pregnancy.

8. 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. 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 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.

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