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PREVENTION OF PLACENTAL DYSFUNCTION IN PREGNANT WOMEN WITH DENTAL PATHOLOGY

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In pregnant women, due to changes in the microbiota, diet, and insufficient oral hygiene, the level of inflammatory markers increases, which can contribute to the dysfunction of the fetoplacental complex. The aim of the study was to assess the impact of dental pathology in pregnant women on the risk of placental dysfunction. We studied 87 pregnant women, including 57 women with pathology of hard tooth tissues and periodontal tissues and 30 pregnant women without signs of dental pathology. The microbiocenosis of the oral cavity, indicators of hormonal, biochemical and biophysical profile, morphological changes in the placenta were studied. A positive correlation between the indicators of oral infection and periodontal pathology ($r=0.58-0.63$, $p<0.05$), as well as the relationship between the increase in C-reactive protein and the increase in periodontal pathology indices ($r=0.58-0.63$, $p<0.05$) was determined. The presence of chronic oral infection was accompanied by a decrease in the content of hormones of the fetoplacental complex, deterioration of the biophysical profile of the fetus and uteroplacental-fetal blood flow, development of hemodynamic and involutinal-dystrophic disorders of the placenta, birth of low-birth-weight children, which confirms the importance of providing timely dental care to prevent placental dysfunction and perinatal complications.

Key words: pregnancy, placenta, periodontium, caries, gingivitis, fetoplacental complex, placental dysfunction.

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ПРОФІЛАКТИКА ПЛАЦЕНТАРНОЇ ДИСФУНКЦІЇ У ВАГІТНИХ ЗІ СТОМАТОЛОГІЧНОЮ ПАТОЛОГІЄЮ

У вагітних внаслідок змін мікробіоти, характеру харчування, недостатнього рівня гігієни порожнини рота, підвищується рівень маркерів запалення, що може сприяти порушенню функціонування фетоплацентарного комплексу. Метою дослідження була оцінка впливу стоматологічної патології у вагітних на ризик розвитку дисфункції плаценти. Досліджено 87 вагітних, в тому числі 57 жінок з патологією твердих тканин зуба та тканин пародонту та 30 вагітних без ознак стоматологічної патології. Вивчали мікробіоценоз порожнини рота, показники гормонального, біохімічного та біофізичного профілю, морфологічні зміни плацент. Визначено позитивний кореляційний зв'язок показників інфікування порожнини рота з патологією пародонта ($r=0,58-0,63$, $p<0,05$), а також зв'язок зростання С-реактивного білка зі збільшенням індексів патології пародонта ($r=0,58-0,63$, $p<0,05$). Наявність хронічної інфекції порожнини рота супроводжувалась зменшенням вмісту гормонів фетоплацентарного комплексу, погіршенням показників біофізичного профілю плода та матково-плацентарно-плодового кровотоку, розвитком гемодинамічних та інволютивно-дистрофічних порушень плацент, народженням дітей з низькою масою тіла, що підтверджує важливість надання своєчасної стоматологічної допомоги вагітним для профілактики дисфункції плаценти та перинатальних ускладнень.

Ключові слова: вагітність, плацента, пародонт, карієс, гінгівіт, фетоплацентарний комплекс, плацентарна дисфункція.

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During pregnancy, a number of functional changes aimed at bearing the fetus occur in a woman's body. In particular, fetal skeleton formation requires a constant fetoplacental supply of osteogenic mineral substances [1]. However, on its own, it does not lead to the loss of calcium from the woman's bone depots; the myth that the fetus consumes calcium mostly from the reserves of the mother's body has long been disproved [8]. Meanwhile, pregnant women have a catabolic orientation of metabolic processes and a decrease in calcium reabsorption in the kidneys combined with decreased calcium absorption in the digestive tract, which causes a violation of calcium metabolism in tissues, including bone [11].

Hypertensive disorders such as preeclampsia and eclampsia, preterm birth are among the leading causes of maternal, early neonatal mortality and child mortality and, especially in low-income countries. Premature babies have a higher risk of respiratory diseases and chronic pathology of the nervous system [11, 12]. Obesity, diabetes, twin pregnancy, teenage pregnancy, and low calcium intake alter this balance and increase the risk of preeclampsia. Calcium deficiency is essential in the pathogenesis of preeclampsia and related disorders. Calcium-containing nutraceuticals improve calcium intake and, as a result, reduce the risk of hypertensive disorders during pregnancy [11].

According to the literature, the frequency of damage to hard dental tissues in pregnant women exceeds the average population levels. The main risk factors are dietary changes, changes in the oral microbiota, and poor hygiene [6].

Recently, the issue of preventing dental caries and providing modern dental care to women during pregnancy and lactation has become quite pressing. Despite the availability of numerous works and

protocols for providing dental care to women during pregnancy, the prevalence of dental diseases remains high [6–10].

Thus, the issue of preventing dental caries and providing modern dental care to women during pregnancy and lactation is relevant.

Among the main causes of disruption of the physiological development of pregnancy are malnutrition and a lack of essential macro- and micronutrients [9–14], mainly in developing countries. The same applies to cases of endemic caries in the case of unfavorable salt composition of drinking water [2].

Dental examination of women is advisable during 6–8, 16–18, 26–28, and 36–38 weeks of pregnancy; treatment and removal of decayed teeth – before pregnancy; if this did not happen, a dental check-up and treatment are to be scheduled between 15 and 22 weeks of gestation (4–14 and 28–32 weeks are considered critical) [7, 15]. At this stage, the fetus has already completed its organogenesis, the placenta has formed, and fetoplacental blood circulation functions; hemodynamics and indices of the mother's immunological status are stabilized [4].

The purpose of the study was to assess the impact of dental pathology in pregnant women on the risk of developing placental dysfunction.

Materials and methods. The study was conducted at the clinical sites of Odesa National Medical University. All patients provided informed consent to participate in the study.

87 pregnant women aged 18 to 39 were examined, including 57 women with the pathology of hard dental tissues and periodontal tissues (experimental group) and 30 pregnant women without signs of dental pathology. The mean age of the examined women was 27.1 ± 0.8 years in the experimental group and 26.7 ± 1.0 years in the control group. 66 women were primigravidae (75.9 %), 61 pregnant women (70.1 %) had a history of abortion.

During 6–8, 16–18, 26–28, and 36–38 weeks of pregnancy, hard dental tissues and oral mucosa were evaluated. The assessment included recording complaints of pain, swelling, hyperemia, bleeding, discomfort, bad breath, history data, and clinical examination. Complaints and clinical symptoms were rated on a 5-point scale: no sign – 0 points, minor – 1 point, moderate – 2 points, pronounced – 3 points, significantly pronounced – 4 points. The following paraclinical indices were determined: Green-Vermillion oral hygiene index (OHIS), Schiller-Pysarev test, PMA index modified by Parma, Muhlemann-Son sulcus bleeding index, and Russell's PI (periodontal index). To assess the intensity of caries, we use the decay-missing-filled (DMF) index for the number of decayed, missing, and restored teeth in one person [15].

The microbiocenosis of the oral cavity was studied in samples of saliva, aspirates of periodontal fluid, detritus of carious lesions, soft dental plaque, and scrapings from the tongue surface. Biomaterial samples were transferred to the blood and yolk-salt MPA using a transport medium for further culture cultivation, the preparation of smears and their Gram staining, and microscopic verification of microorganisms [7].

Diagnosis of placental dysfunction was performed by determining the levels of the hormones estriol, progesterone, and placental lactogen; ultrasound assessment of the placenta, the degree of its maturity; Doppler blood flow of the fetoplacental complex; fetal biophysical profile, morphological examination of the placentas [4].

Ultrasound examination (ultrasound) was performed using a Toshiba NEMIO scanner (Japan) using transabdominal and transvaginal sensors with a frequency of 3.5 MHz. Fetal cardiac activity was assessed from 28–30 weeks of gestation using the Feta RPT BMT 9141 Neasa device in real time for 30 minutes at a tape speed of 1 cm/min. During Doppler blood flow in the uterine arteries, umbilical cord artery and fetal aorta, the systolic-diastolic ratio (SDR), resistance index (RI) and pulsatile index (PI) were evaluated.

Placentas of parturient women were studied; the material was fixed in 10 % neutral formalin with further processing according to the standard, generally accepted unified methodology. Histological preparations were examined under an OLYMPUS light microscope at a magnification of x100 (eyepiece x 10, objective x 10) [1].

The study was performed in compliance with current bioethical requirements [3].

Statistical processing was carried out by dispersion and correlation analysis using MS Excel software (Microsoft Inc., USA).

Results of the study and their discussion. All pregnant women in the experimental group required dental care. The prevalence of dental caries was 96.4 % on average, and 2.14 teeth per woman needed filling. The intensity of the increase in dental caries during the gestation and lactation periods ranged from 0.52 to 1.96 teeth per examined woman. Almost half of the pregnant women studied had secondary caries and damage to previously intact teeth, mainly with an acute course of the carious process. A clinical feature of

the course of the carious process in pregnant women is the rapid spread both along the peripheral areas and in the depth of tooth tissues (56 %), which, in a short time, leads to the development of complicated caries.

Among the women in the experimental group, there were 12 (21 %) women examined in the first trimester of pregnancy, 27 (47.36 %) – in the second trimester, and 18 (31.57 %) – in the third trimester. Among women in the control group, the distribution by trimester was as follows: 9 (30.0 %), 13 (43.3 %) and 8 (26.7 %) ($p>0.05$).

Therefore, an essential part of the sanitary and educational work of dentists and, above all, gynecologists are explaining the importance of timely referral of pregnant women to a dentist for timely oral sanitation. The result of such sanitary and educational work should be a significantly decreased number of pregnant women visiting the dentist in the last stages of pregnancy.

According to the results of the survey, 17 women (30.00 %) regularly had their teeth treated before pregnancy, 3 (17.64 %) – because of acute tooth pain, and 3 (17.64 %) – to prepare for pregnancy. 24 (42.1 %) women underwent dental treatment during pregnancy, 6 (25 %) of them – in the 1st trimester, 8 (33.3 %) – in the 2nd trimester, and 9 (37.5 %) – in the 3rd trimester of pregnancy.

Evaluation of clinical signs and complaints of the oral cavity using a scoring system in the experimental group gave the following results: pain – 1.8 ± 0.35 ; discomfort – 2.7 ± 0.1 ; edema – 2.7 ± 0.16 ; hyperemia – 2.9 ± 0.47 ; bleeding – 2.3 ± 0.24 ; bad breath – 3.8 ± 0.94 . In the control group, these manifestations were not detected ($p<0.001$).

The condition of periodontal tissues according to hygiene indices: OHIS – 2.9 ± 0.26 ; Schiller-Pysarev test – 4.5 ± 0.35 ; PMA index modified by Parma – 57.22 ± 6.45 %; Muhlemann-Son sulcus bleeding index – 2.8 ± 0.35 ; Russell's PI – 2.15 ± 0.27 . No signs of periodontal pathology were found in the control group, and the OHIS index did not exceed 0.7 ± 0.06 ($p<0.01$).

Table 1

The qualitative composition of oral cavity microbiocenosis in pregnant women in both clinical groups

Microorganisms	Experimental group (n=57)	Control group (n=30)
S. mutans	+	-
Veillonella	+	+
Lactobacillus	+	+
Bifidobacterium	+	+
Propionibacterium	+	-
Actinomyces spp	+	-
Atopobium sp	+	-
P. gingivalis	+	+
T. forsythensis	+	-
T. denticola	+	+
P. intermedia	+	-
F. nucleatum	+	+
P. nigrescens	+	-
C. Rectus	+	-
S. sobrinus	+	+
S. sanguinus,	+	+
L. acidophilus	+	+
L. casei,	+	+
A. naeslundii	+	
A. actinomycetemcomitans	+	
R. Micra	+	
Peptosreptococcus	+	
Propionebacteria,	+	
Mobiluncus	+	
Candidaspp	+	

Assessing the state of the oral cavity microbiocenosis showed that in women with carious lesions, S. mutans and other microorganisms associated with inflammatory and destructive changes in hard dental tissues (Veillonella, Lactobacillus, Bifidobacterium, Propionibacterium, Actinomyces pp., Atomycess pp.) predominated. In pregnant women with pigmented soft dental plaque, microorganisms of the “red cluster” (P. gingivalis, T. forsythensis, T. denticola) and the “orange cluster” (F. nucleatum, P. intermedia, P. nigrescens, C. Rectus) were detected. Other cultured microorganisms included S. sobrinus, S.

sanguinus, L. acidophilus, L. casei, A. naeslundii, A. actinomycetem comitans, P. micra, Peptoscryptococcus, Propionebacterium, Mobiluncus, Candidasp.

Pregnant women in the control group had significantly fewer opportunistic pathogens; obligate and facultative anaerobic streptococci prevailed in their microbiocenosis structure (Table 1).

Ultrasound examination of pregnant women in the main group revealed signs of placental dysfunction in 32 patients (56.1 %): premature maturation in 11 (19.3 %), dystrophic changes in 8 (14.0 %), pathological immaturity in 4 (7.0 %), the discrepancy in placental thickness to gestational age in 6 (10.5 %), and placental edema in 3 (5.3 %). No pathological changes in the placenta were noted in the control group.

Indices of the fetal biophysical profile at 32–34 weeks of gestation in the main group were significantly lower (7.55 ± 0.14) than in the control group (8.56 ± 0.12) ($p < 0.01$). Doppler examination of pregnant women in the main group revealed a significant increase in the systolic-diastolic ratio in the uterine arteries (3.25 ± 0.14) vs. 2.3 ± 0.12 vs. 5.72 ± 0.15 in the control (all differences are significant), which indicated a violation of the hemodynamics of the fetoplacental complex, disruption of the adaptation of the mother's compensatory and adaptive mechanisms to pregnancy.

Table 2 shows the levels of fetoplacental complex hormones and C-reactive protein in the blood plasma of pregnant women of both clinical groups. As can be seen, a significant decrease in the levels of estriol, progesterone and placental lactogen ($p < 0.05$) and an increase in the levels of inflammatory markers were observed in pregnant women of the main group at 32–34 weeks, indicating placental dysfunction.

Table 2

Hormonal and biochemical profile of pregnant women in both clinical groups

Indices	Experimental group (n=57)		Control group (n=30)	
	20–22 weeks	32–34 weeks	20–22 weeks	32–34 weeks
Estriol, nmol/l	78.2±1.4	88.8±2.9*	84.1±2.8	110.9±3.3
Progesterone, nmol/l	380.6±11.5*	434.4±12.4*	560.8±15.3	626.3±14.9
Placental lactogen, nmol/l	201.4±13.5	210.3±10.6*	220.7±12.8	259.8±11.1
CRP, mg/l	6.4±0.1*	7.8±0.1*	3.8±0.2	4.1±0.1

Note: * – differences between groups are statistically significant ($p < 0.05$)

All pregnant women gave birth to live children, the Apgar score at the first minute was 7.5 ± 0.1 points in the main group and 8.5 ± 0.2 points in the control group ($p < 0.05$); women in the main group had cases of preterm birth in 3 (5.3 %) cases, fetal growth retardation in 5 (8.8 %) cases, newborn conjugal jaundice in 18 (31.6 %) cases, perinatal hypoxic central nervous system damage in 6 (10.5 %) cases. In the control group, there were only cases of conjugal jaundice in 7 (23.3 %) newborns.

Figures 1–4 show histological changes in the placenta in pregnant women with signs of dental pathology. Regardless of the age of the pregnant woman, in the late stages of gestation, changes in the villous chorion occur in the form of calcium accumulation, which can be considered a manifestation of placental dysfunction (Fig.1).

Examination of the placenta detected inflammatory changes in the stroma of the villi and the intervillous space. Inflammatory infiltrates consisted mainly of polymorphonuclear neutrophil leukocytes (Fig. 2).

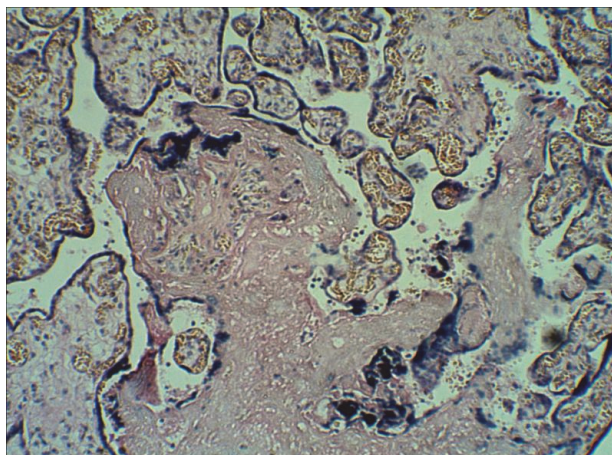


Fig. 1. Placenta of a 37-year-old woman. Pregnancy – 40 weeks. Petrified of the villous chorion. Hematoxylin and eosin staining. Ob x10, Oc x10.

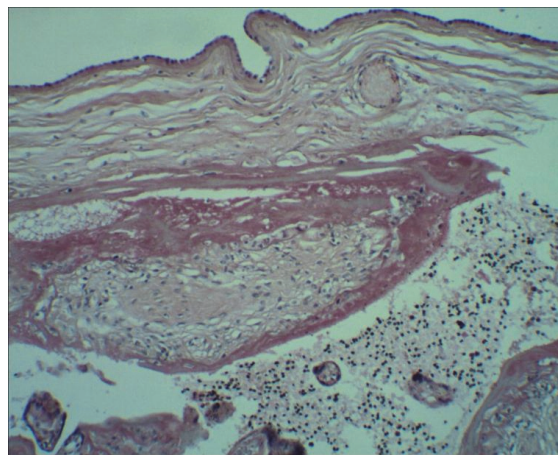


Fig. 2. Placenta of a 27-year-old woman. Pregnancy – 34 weeks. Villitis and intervillitis. Hematoxylin and eosin staining. Ob x10, Oc x10.

Hemodynamic disorders were in the form of hemorrhages in the stroma of the chorionic villi, the intervillous space, hyperemia of the villi, and uneven blood filling of the vessels of the terminal villi (Fig.3).

Fibrinoid accumulations were present in the villous stroma and the intervillous space. They were located around the terminal villi and glued (Fig. 4).

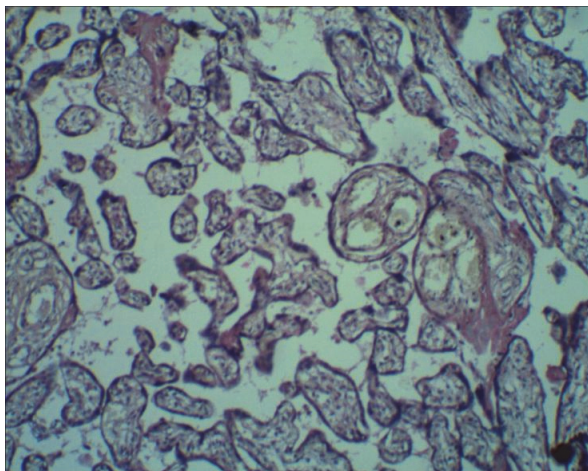


Fig. 3. Placenta of a 31-year-old woman. Pregnancy 32 weeks. Uneven blood filling of terminal villi vessels. Hematoxylin and eosin staining. Ob x10, Oc x 10.

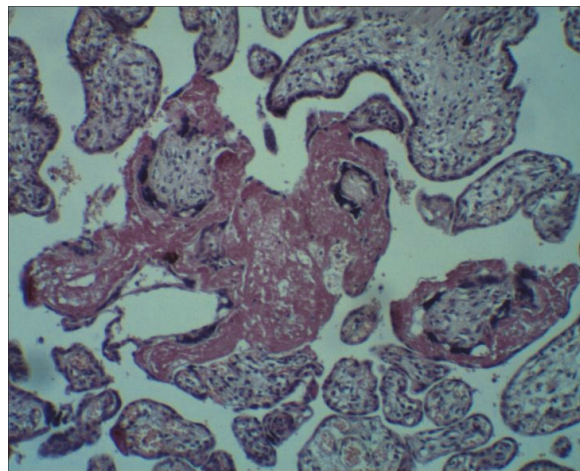


Fig. 4. Placenta of a 27-year-old woman. Pregnancy – 28 weeks. Fibrinoid glues the villi of the chorion. Hematoxylin and eosin staining. Ob x10, Oc x10.

In pregnant women with reduced levels of estriol, progesterone and placental lactogen, the gums react more strongly to the action of microorganisms, particularly *P. gingivalis* and *P. intermedia*. Pregnant women with *P. gingivalis* had increased gum inflammation ($p < 0.001$), which was not associated with dental plaque [7].

In pregnant women of the experimental group with signs of periodontal tissue pathology (OHIS = 2.9 and PMA = 57.22 %), there was an increase in the concentration of C-reactive protein in the plasma (up to 7.8 ± 0.1 mg/l) versus 4.1 ± 0.1 in the control group; $p < 0.05$) between 32 and 35 weeks of pregnancy. A positive correlation with indices of periodontal pathology was realized ($r = 0.58 - 0.63$, $p < 0.05$).

The interdependence of the condition of the oral tissues and the fetoplacental complex observed in this study can be due to the following. During pregnancy, the hormonal balance of pregnant women changes. Many tissues undergo some changes as the placenta produces higher levels of estrogen and progesterone during pregnancy. During this period, excessive sensitivity of the gums to irritation occurs. During pregnancy, gingivitis or epulis gravidarum can often occur. Gingivitis during pregnancy usually begins in the second month of pregnancy, reaches the highest degree of severity in the eighth month, and heals spontaneously after childbirth. According to various authors, gingivitis in pregnant women occurs in 30–50 % of pregnancies [15].

Women with healthy gums are likely to have a minimal risk of developing gingivitis [5, 14]. However, in the presence of a traumatic impact, vitamin C deficiency, or poor hygiene conditions arise for periodontal tissue damage, as to the development of placental dysfunction which in turn can increase the risk of gestational complications and the birth of children small for gestational age [10, 15]. It is of great significance to consider that chronic inflammation in the oral cavity activates oxidative stress and accordingly triggers mechanisms of endothelial dysfunction, ultimately leading to placental dysfunction [9].

There is no scientific proof for the statement that calcium, necessary for fetus intrauterine development, is obtained from the mother's teeth and that each pregnancy is associated with tooth loss [9, 10]. The increased frequency of damage to the hard dental tissues in pregnant women has another explanation. Nausea and vomiting are observed in 70 % of pregnant women [6, 15]. Vomiting can negatively affect oral hygiene or cause enamel erosion in pregnant women. Maintaining good oral hygiene during pregnancy can help prevent this problem.

Deterioration of the oral cavity's condition and teeth during pregnancy depends on the following factors [13]: increased consumption of sweets, neglected tooth brushing, increased bacterial plaque, frequent bleeding from the gums, and frequent vomiting. These factors create an acidic environment and decrease saliva flow, promoting the progression of caries. However, good oral hygiene practices can eliminate all these factors [8, 10–12, 14].

Conclusions

1. In all trimesters of pregnancy, the highest prevalence of gingivitis is observed among women with an unsatisfactory level of oral hygiene index. In pregnant women, decreased levels of estriol, progesterone and placental lactogen in the third trimester of pregnancy are inversely correlated with the presence of *P. gingivalis* and *P. intermedia* and increased gingival inflammation. The deterioration of periodontal tissues, including the oral hygiene index OHI-S (2.9) and PMA (57.22 %) between 32 and 35 weeks of pregnancy correlates with an increase in plasma C-reactive protein. A positive correlation was found between the increase in C-reactive protein and the increase in periodontal pathology indices ($r=0.58-0.63$, $p<0.05$).

2. The presence of chronic oral infection could be a trigger for the development of placental dysfunction, which was manifested by morphological changes in the placenta (increased accumulation of calcium salts in the villous chorion, the presence of villusitis and intervillitis, increased fibrinide content in the intervillous space, hemodynamic and involutinal-dystrophic changes), a drop in the content of fetoplacental complex hormones and was realized in the form of uteroplacental-fetal blood flow disorders, deterioration of fetal biophysical profile and ultrasound placentometry, birth of low birth weight babies, perinatal hypoxic central nervous system damage.

3. Comprehensive management of pregnant women to prevent placental dysfunction includes mandatory preventive dental care and close interprofessional cooperation between family doctor, dentist, and obstetrician-gynecologist.

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