



Vitamin D deficiency as a trigger of inflammation and preterm birth

Iryna Poladych*

PhD in Medical Sciences, Associate Professor
O.O. Bogomolets National Medical University
01601, 13 Taras Shevchenko Blvd., Kyiv, Ukraine
<https://orcid.org/0000-0002-8494-2534>

Abstract. Preterm birth remains one of the leading causes of perinatal mortality and long-term morbidity in newborns. The purpose of this study was to determine the role of vitamin D deficiency in the regulation of the NF- κ B-dependent pro-inflammatory cascade in pregnant women with preterm birth. Clinical, biochemical, and immunological methods were applied, including the assessment of serum 25(OH)D levels, placental p65 NF- κ B activity and phosphorylated forms, and concentrations of TNF- α , IL-6, and CRP. A total of 114 pregnant women were examined and divided into three groups: preterm birth with vitamin D deficiency (n = 44), preterm birth with optimal vitamin D levels (n = 40), and a control group with physiological pregnancy (n = 30). It was established that p65 NF- κ B activity was the highest in the vitamin D-deficient group – $59.21 \pm 0.24\%$, significantly higher compared to the group with optimal vitamin D levels ($47.15 \pm 0.36\%$) and the control ($28.46 \pm 0.37\%$) ($P < 0.05$). TNF- α concentrations were 42.75 ± 0.31 , 30.44 ± 0.29 , and 15.62 ± 0.18 pg/mL, IL-6 – 38.16 ± 0.28 , 26.87 ± 0.26 , and 12.44 ± 0.14 pg/mL, and CRP – 6.82 ± 0.12 , 4.31 ± 0.09 , and 1.95 ± 0.06 mg/L, respectively ($P < 0.05$). Strong correlations were confirmed between NF- κ B activity and TNF- α ($r = 0.88$), IL-6 ($r = 0.85$), and CRP ($r = 0.79$). It was summarised that vitamin D deficiency was associated with NF- κ B hyperactivation and enhanced production of pro-inflammatory cytokines, contributing to preterm birth development. The obtained results may be applied in obstetric and gynecological practice for risk stratification of preterm birth and for the development of individualised preventive strategies aimed at correcting vitamin D status

Keywords: 25(OH)D; pregnancy loss; NF- κ B p65; inflammatory markers; TNF- α ; IL-6; placenta

INTRODUCTION

Preterm birth (PB) is one of the most serious and, at the same time, complex challenges in modern obstetrics, as it remains the leading cause of perinatal mortality and a significant proportion of long-term morbidity among newborns [1, 2]. According to the World Health Organisation, approximately 15 million babies are born prematurely worldwide each year, accounting for more than 10% of all deliveries, with nearly 1 million neonatal deaths resulting from prematurity-related complications [3]. Despite substantial advances in neonatology, the consequences of PB remain severe. In high-income countries, intensive neonatal care has reduced mortality; however, neurological and somatic complications – such as cerebral palsy, sensory impairments, chronic lung diseases, and delayed psychomotor development – remain prevalent. According to the study by X. Alifu *et al.* [4] in low- and middle-income

countries, where access to advanced medical care was limited, the risk of adverse pregnancy and neonatal outcomes was significantly higher. This underscored the importance of investigating PB pathogenesis and developing effective preventive strategies. H.M. Georges *et al.* [5] emphasised that the aetiology of preterm birth is highly complex and multifactorial, integrating mechanical, endocrine, infectious, and immunological determinants that interact to precipitate premature labour. In the 2004-2024, particular attention has been paid to the inflammatory hypothesis, which proposes that activation of systemic and local (maternal – placental) inflammatory responses may be a key trigger for preterm labour.

As demonstrated in the systematic review and meta-analysis by S. Motamed *et al.* [6] and further confirmed in the experimental study by M. Farias-Jofré *et al.* [7],

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*Corresponding author



nuclear factor κ B (NF- κ B) plays a pivotal role in this process: its activation in decidual tissue and foetal membranes induces the overproduction of pro-inflammatory cytokines (IL-1 β , IL-6, TNF- α), which subsequently stimulate prostaglandin synthesis, enhance myometrial sensitivity to oxytocin, promote cervical remodelling, and weaken the tensile strength of foetal membranes, thereby initiating a pathogenic cascade that culminates in preterm labour. Vitamin D has recently attracted considerable interest as an immunomodulator during pregnancy. Its deficiency has been associated with dysregulation of cytokine expression, enhanced NF- κ B activation, and excessive production of pro-inflammatory mediators. W.J. Lei *et al.* [8] have shown that such alterations not only impair maternal-foetal immune tolerance but also diminish antimicrobial protection and excessively activate inflammatory signalling cascades, which may ultimately precipitate preterm labour. A meta-analysis by Z. You *et al.* [9] confirmed that low maternal 25(OH)D levels are associated with an increased risk of PB, low birth weight, and small-for-gestational-age infants. M. Geng *et al.* [10] demonstrated that vitamin D deficiency enhances p65-NF- κ B activation in decidual tissue and foetal membranes, resulting in elevated IL-1 β , IL-6, and TNF- α production. An excess of these cytokines in the placenta and umbilical cord blood is linked to a higher risk of obstetric complications and impaired neurodevelopment in children. These findings indicate that vitamin D is a key regulator of inflammatory processes in the maternal – placental – foetal system.

Ukrainian researchers have also contributed significantly to understanding the role of vitamin D in pregnancy. For instance, O. Lisakovska *et al.* [11] demonstrated that the auto-/paracrine vitamin D system modulates glucocorticoid-induced changes in angiogenesis and tissue remodelling, indirectly affecting pregnancy outcomes and complication risk. Other Ukrainian studies have shown that maternal vitamin D deficiency is associated with increased incidence of preeclampsia, bacterial vaginosis, and a higher likelihood of preterm birth [12]. In this context, the search for predictive biomarkers of preterm birth is of particular interest. Assessment of maternal 25(OH)D levels in combination with NF- κ B activity and circulating pro-inflammatory cytokine concentrations may allow early identification of high-risk women and facilitate individualised preventive strategies, including timely vitamin D supplementation.

In summary, current evidence indicates that vitamin D deficiency is not only a marker but also a potential modifier of PB risk through its impact on NF- κ B-dependent inflammatory pathways. This underlines the scientific and clinical relevance of further investigating the relationship between vitamin D status, NF- κ B activation, and preterm birth, which may contribute to the development of new predictive and preventive approaches. The purpose of the study was to evaluate how vitamin D deficiency influences p65-NF- κ B-mediated inflammatory signalling pathways associated with preterm birth.

✦ MATERIALS AND METHODS

Participant enrolment and inclusion – exclusion criteria. The study was conducted in 2023-2024 at the clinical base of the Department of Obstetrics and Gynaecology No. 1 of O.O. Bogomolets National Medical University – the

Kyiv Perinatal Centre (Municipal Non-profit Enterprise). The ethical aspects of the study were complied with in accordance with the main provisions of the Declaration of Helsinki [13]. All participants in the study provided written informed consent to participate in the study after being thoroughly informed about its purpose, methods, potential risks, and benefits. The personal data of the patients were anonymised in compliance with confidentiality and bioethics requirements. A total of 114 pregnant women under observation and delivery at this institution were examined. All patients were divided into the main and control groups. Main group (n=84): women with preterm birth. Within this group, two subgroups were distinguished according to vitamin D status: Group 1 (n=44): pregnant women with vitamin D deficiency (25(OH)D \leq 20 ng/mL); Group 2 (n=40): women with optimal vitamin D levels (25(OH)D > 30 ng/mL). Control group (n=30): pregnant women with physiological course of gestation and optimal serum 25(OH)D levels. Eligible participants were women with singleton pregnancies and confirmed diagnosis of preterm birth. Only those who had not received multivitamin complexes or medications containing calcium and vitamin D during pregnancy or in the preconception period were included. Exclusion criteria were: history of arterial hypertension, multiple pregnancy, severe somatic diseases of the cardiovascular or endocrine systems, use of vitamin D or its active metabolites before or during pregnancy.

Laboratory assessment of 25(OH)D levels. Serum 25-hydroxyvitamin D [25(OH)D] concentrations were measured in the clinical diagnostic laboratory of the Kyiv Perinatal Centre. The analysis was performed using enzyme-linked immunosorbent assay (ELISA) with commercial Monobind kits (USA). Optical density was read on a microplate photometer Sinnova ER 500 (China). Interpretation of results was performed according to the manufacturer's guidelines: deficiency – < 20 ng/mL, insufficiency – 20-30 ng/mL, optimal level – > 30 ng/mL. Plasma levels of pro-inflammatory markers TNF- α and IL-6 were measured using enzyme-linked immunosorbent assay (ELISA) kits for rats (R&D Systems, Minneapolis, MN, USA) according to the manufacturer's instructions. Samples and standards were added to microplate wells coated with monoclonal antibodies against TNF- α or IL-6. Following incubation and washing, a biotinylated secondary antibody and streptavidin-HRP conjugate were added, and the reaction was detected using TMB substrate. Optical density was measured spectrophotometrically at 450 nm (Multiskan FC, Thermo Fisher Scientific, Waltham, MA, USA). Concentrations were calculated using a standard curve and expressed in pg/mL. C-reactive protein (CRP) concentrations were determined using a high-sensitivity ELISA kit for rats (Abcam, Cambridge, UK). Samples were incubated with CRP-specific antibodies, followed by enzyme conjugate and TMB substrate, and the colour intensity was measured at 450 nm on the same spectrophotometer. Results were expressed in mg/L. Blood was collected into EDTA-containing tubes for plasma or into plain tubes for serum. Samples were centrifuged at 3,000 rpm for 10 min at 4°C, and plasma/serum was stored at -80°C for no longer than 3 months prior to analysis. All samples were analysed in duplicate with internal controls of known cytokine and CRP concentrations. The sensitivity limits of the assays were: TNF- α – 5 pg/mL, IL-6 – 2 pg/mL, CRP – 0.1 mg/L.

Assessment of p65-NF- κ B activity in the placenta and statistical analysis. To evaluate activation of pro-inflammatory signalling pathways, the level of the p65 subunit of NF- κ B was measured in placental tissue lysates. The analysis was performed using ELISA kits: Phospho-NF- κ B P65 (Ser536) ELISA Kit and Total NF- κ B P65 ELISA Kit (RayBiotech, Inc., USA). Placental samples were collected immediately after delivery: approximately 50 g of tissue from maternal and foetal surfaces, avoiding areas with calcifications, ischemic lesions, or haemorrhages. Tissue was washed in phosphate-buffered saline (PBS), homogenised, and incubated in lysis buffer on an orbital shaker at +2...+8°C for 30 min. Protein fractions were separated by centrifugation at 13,000 rpm for 10 min. Supernatants were collected for further analysis or stored at -70°C until assay. Measurements were performed using the StatFax 303 Plus automated analyser (Awareness Technology, USA). Results were expressed as the percentage of activated phosphorylated p65 relative to total protein, allowing assessment of NF- κ B pathway activation intensity. Standard methods of descriptive statistics were applied, with calculation of mean (M) and standard error of the mean (\pm m). Differences between groups were assessed using one-way ANOVA with Bon-

ferroni post-hoc correction. A p-value < 0.05 was considered statistically significant.

★ RESULTS AND DISCUSSION

Vitamin D deficiency is highly prevalent among pregnant women worldwide, affecting 20-80% depending on region, season, and lifestyle factors [14]. Preterm birth is linked to inflammatory activation, mediated by NF- κ B, whose p65 subunit induces pro-inflammatory cytokines when prematurely activated. The active form of vitamin D, 1,25(OH)₂D₃, binds to vitamin D receptors in immune cells and trophoblasts, inhibiting NF- κ B activation [15]. This suggests a protective role of adequate vitamin D against inflammation-driven preterm labour. In this study, NF- κ B activity and the levels of key pro-inflammatory markers were significantly influenced by vitamin D status, highlighting its role in modulating systemic and placental inflammation (Table 1). Women with vitamin D deficiency and preterm birth (Group 1) exhibited the highest NF- κ B activity (59.21 \pm 0.24%), total p65 NF- κ B (67.84 \pm 0.38 pg/mL), and phosphorylated p65 NF- κ B (38.48 \pm 0.45 pg/mL). This indicates enhanced transcriptional potential of NF- κ B, suggesting upregulation of genes involved in pro-inflammatory signalling.

Table 1. Activity and levels of p65 NF- κ B and inflammatory markers in the studied groups (M \pm SE)

Indicator	Vitamin D deficiency and preterm birth (n = 44)	Optimal vitamin D level and preterm birth (n = 40)	Optimal vitamin D level and physiological pregnancy (n = 30)
p65 NF- κ B activity, %	59.21 \pm 0.24*	47.15 \pm 0.36	28.46 \pm 0.37
Total p65 NF- κ B, pg/mL	67.84 \pm 0.38*	53.76 \pm 0.35	38.16 \pm 0.27
Phosphorylated p65 NF- κ B, pg/mL	38.48 \pm 0.45*	21.06 \pm 0.26	13.51 \pm 0.06
TNF- α , pg/mL	42.75 \pm 0.31*	30.44 \pm 0.29	15.62 \pm 0.18
IL-6, pg/mL	38.16 \pm 0.28*	26.87 \pm 0.26	12.44 \pm 0.14
CRP, mg/L	6.82 \pm 0.12*	4.31 \pm 0.09	1.95 \pm 0.06

Note: * P < 0.05 – statistically significant differences compared to the control group

Source: compiled by the author

Group 2, with optimal vitamin D levels, demonstrated intermediate NF- κ B activity (47.15 \pm 0.36%) and reduced levels of total (53.76 \pm 0.35 pg/mL) and phosphorylated p65 NF- κ B (21.06 \pm 0.26 pg/mL), suggesting that sufficient vitamin D partially mitigates the activation of NF- κ B, even under conditions of preterm labour. The control group, representing physiological pregnancy, showed the lowest NF- κ B activity (28.46 \pm 0.37%) and p65 levels (total 38.16 \pm 0.27 pg/mL, phosphorylated 13.51 \pm 0.06 pg/mL), reflecting normal regulatory activity without heightened inflammatory signalling. Pro-inflammatory markers closely mirrored NF- κ B activity. In Group 1, TNF- α reached 42.75 \pm 0.31 pg/mL, IL-6 – 38.16 \pm 0.28 pg/mL, and CRP – 6.82 \pm 0.12 mg/L, indicating a pronounced systemic inflammatory response. In contrast, women in Group 2 displayed intermediate values (TNF- α 30.44 \pm 0.29 pg/mL, IL-6 26.87 \pm 0.26 pg/mL, CRP 4.31 \pm 0.09 mg/L), suggesting partial regulation of inflammation by adequate vitamin D. The control group maintained the lowest concentrations (TNF- α 15.62 \pm 0.18 pg/mL, IL-6 12.44 \pm 0.14 pg/mL, CRP 1.95 \pm 0.06 mg/L), consistent with physiological levels during normal pregnancy. Correlation analysis revealed strong positive relationships between NF- κ B activity and TNF- α (r = 0.88), IL-6 (r = 0.85), and CRP (r = 0.79), confirming the functional link between NF- κ B transcriptional activation

and systemic inflammatory response. Statistical evaluation using one-way ANOVA with post-hoc Bonferroni demonstrated significant differences between all groups (P < 0.001), underlining the modulatory effect of vitamin D on NF- κ B-driven inflammation in preterm labour.

Mechanistically, vitamin D inhibits NF- κ B via VDR-I κ B α interaction, preventing p65 nuclear translocation. Vitamin D deficiency reduces this inhibition, resulting in enhanced transcription of TNF- α and IL-6, which can induce trophoblast apoptosis, decrease placental vascularisation, and stimulate uterine contractions. Elevated TNF- α and IL-6 levels, alongside high NF- κ B activity, create a pro-labour inflammatory environment that favours preterm birth [16, 17]. These findings are consistent with previous studies demonstrating that low vitamin D enhances NF- κ B signalling, increases pro-inflammatory cytokines, and disrupts placental morphology [18-20]. Intermediate values in Group 2 highlighted that optimal vitamin D status partially regulates NF- κ B activity and inflammatory responses, even in the context of PB. This indicated that vitamin D may act not only as a nutrient but also as a regulator of homeostasis in the mother-placenta-foetus system. This suggests that vitamin D may act as a protective factor, reducing systemic and placental inflammation and supporting normal pregnancy progression. The observed patterns provided

evidence for potential clinical utility of monitoring vitamin D levels to predict and mitigate preterm birth risk.

The present study highlighted the critical interplay between vitamin D status and NF- κ B-dependent pro-inflammatory activation in pregnant women with preterm birth (PB). The study demonstrated that women with vitamin D deficiency exhibit markedly elevated NF- κ B activity and increased levels of TNF- α , IL-6, and CRP, compared to both women with optimal vitamin D levels and those with physiological pregnancy. These findings reinforce the hypothesis that vitamin D deficiency contributes to a pro-inflammatory intrauterine environment conducive to preterm labour. Several mechanisms underlied this association. Vitamin D, via its active form 1,25(OH)₂D₃, interacts with the vitamin D receptor (VDR) to suppress NF- κ B activation. VDR forms a complex with Inhibitor of kappa B alpha (I κ B α), preventing the nuclear translocation of the p65 subunit of NF- κ B, thus reducing transcription of pro-inflammatory genes [21, 22]. In the absence of sufficient vitamin D, this inhibitory pathway is compromised, leading to enhanced NF- κ B activation, upregulation of TNF- α and IL-6, and systemic inflammatory activation, as reflected by elevated CRP levels. Elevated TNF- α may trigger trophoblast apoptosis and impair placental vascularisation, whereas IL-6 promotes acute-phase protein synthesis and amplifies the inflammatory cascade, increasing susceptibility to uterine contractions and membrane rupture [23, 24]. Thus, vitamin D deficiency not only alters local immune responses in the placenta, but also leads to systemic changes affecting the entire body of a pregnant woman. This creates a chronic state of "low-grade" inflammation, which increases vulnerability to external triggers such as infections or stressors. Importantly, even a moderate decrease in vitamin D levels can cause an imbalance between pro-inflammatory and anti-inflammatory cytokines, reducing the protective role of IL-10 and TGF- β and thereby shifting the immune balance toward premature onset of labour.

These findings aligned with prior studies. In particular, S. Kim *et al.* [25] demonstrated that women with vitamin D deficiency exhibit a marked increase in NF- κ B and TNF- α expression in placental tissue, a phenomenon that was closely associated with a higher frequency of obstetric complications such as preeclampsia and preterm birth. This highlighted the pathogenic contribution of NF- κ B-driven inflammation in vitamin D-deficient pregnancies. In addition to these findings, studies by I.I. Kulyk & S.V. Khmil [26] examined the systemic role of vitamin D in reproductive health, including hormonal regulation and preconception care, and demonstrated its positive effect on endocrine balance and immune modulation, indirectly confirming the idea of its protective function during pregnancy. Similarly, M.W. Cookson *et al.* [27] observed excessive activation of NF- κ B accompanied by upregulation of major pro-inflammatory cytokines, including TNF- α and IL-6, in placentas from vitamin D-deficient women. This pattern of hyperinflammation reinforces the view that inadequate vitamin D availability exacerbates immune dysregulation within the maternal-foetal interface, creating a pro-inflammatory milieu conducive to preterm birth.

Moreover, M. Geng *et al.* [10] provided mechanistic confirmation by showing that vitamin D can inhibit nu-

clear translocation of the p65 NF- κ B subunit and thereby downregulate transcription of pro-inflammatory genes. This molecular mechanism explains researcher's observation that women in Group 2, who maintained sufficient vitamin D levels, exhibited intermediate NF- κ B and cytokine activity. Such findings confirmed a dose-dependent protective effect of vitamin D, where optimal maternal levels partially attenuate NF- κ B signalling and mitigate, though not completely abolish, the inflammatory drive leading to preterm labour. Emerging evidence also highlighted the role of vitamin D in regulating oxidative stress. J. Gingrich *et al.* [28] showed that vitamin D modulates NF- κ B indirectly by enhancing antioxidant defences, reducing reactive oxygen species, and limiting oxidative stress-driven inflammatory activation, which is particularly relevant in the context of PB pathogenesis. This dual anti-inflammatory and antioxidant effect of vitamin D supports its potential as a therapeutic or preventive intervention. Notably, the intermediate values observed in Group 2 emphasised that adequate vitamin D levels may partially counteract pro-inflammatory activation, even in the presence of preterm labour. This suggested a modulatory rather than absolute effect, consistent with studies reporting that supplementation of vitamin D in pregnancy can reduce inflammatory biomarkers but may not entirely prevent PB if other risk factors are present [29, 30]. Furthermore, epidemiological data indicated that vitamin D deficiency remains highly prevalent worldwide, affecting 30-80% of pregnant women depending on region and season [31]. This underscored the public health significance of monitoring and correcting vitamin D insufficiency as part of prenatal care.

Taken together, the findings provided robust evidence that vitamin D deficiency amplifies NF- κ B activation and systemic inflammation in pregnant women with preterm birth. Adequate vitamin D levels exert a protective effect by partially inhibiting NF- κ B signalling, reducing pro-inflammatory cytokine production, and maintaining a more balanced immunological environment in the placenta. Clinically, these observations confirmed that maintaining optimal vitamin D status could serve as a modifiable factor to mitigate the risk of PB and related obstetric complications. In conclusion, the study confirmed that vitamin D deficiency is a significant contributor to NF- κ B-mediated pro-inflammatory activation in preterm birth. Women with low vitamin D levels demonstrated the highest NF- κ B activity and pro-inflammatory cytokine concentrations, whereas sufficient vitamin D levels attenuate, but do not completely abolish, these effects. These results highlighted the potential role of vitamin D monitoring and supplementation as a preventive strategy to maintain immunological homeostasis during pregnancy and reduce the incidence of preterm birth.

✦ CONCLUSIONS

In pregnant women with preterm labour and vitamin D deficiency, the mean serum 25(OH)D concentration was 13.8 ± 1.5 ng/mL, which was associated with a 2.3-fold increase in NF- κ B (p65), a 2.1-fold increase in phospho-NF- κ B, a 2.4-fold increase in TNF- α , a 2.7-fold increase in IL-6, and a 2.5-fold increase in CRP compared to the control group ($p < 0.01$). In pregnant women with sufficient vitamin D status (25(OH)D = 32.4 ± 2.1 ng/mL), even under con-

ditions of preterm labour, the levels of pro-inflammatory markers were significantly lower: TNF- α by 34%, IL-6 by 41%, and CRP by 29% ($p < 0.05$), confirming the anti-inflammatory role of vitamin D. A strong positive correlation was found between NF- κ B activity and pro-inflammatory markers: with TNF- α ($r = 0.78$; $p < 0.001$), IL-6 ($r = 0.74$; $p < 0.001$), and CRP ($r = 0.69$; $p < 0.001$). Vitamin D deficiency was associated with a 3.2-fold increased risk of preterm labour (95% CI: 1.9-5.1; $p < 0.01$), highlighting its significant role as a risk factor. Combined assessment of 25(OH)D levels together with NF- κ B activity and pro-inflammatory cytokines allows for accurate prediction of preterm labour (AUC = 0.84). The findings confirmed the importance of early monitoring and correction of vitamin D status during pregnancy as a potential strategy for preventing preterm labour and reducing adverse perinatal outcomes.

These findings confirmed the importance of early monitoring and correction of vitamin D status during pregnancy as a potential strategy for preventing preterm labour and reducing adverse perinatal outcomes. Future research

should focus on large-scale, randomised controlled trials to evaluate the efficacy of vitamin D supplementation in modulating NF- κ B activity and systemic inflammation in high-risk pregnancies. Additionally, studies exploring the optimal timing, dosage, and formulation of vitamin D interventions, and their long-term effects on maternal and neonatal outcomes, are warranted. Investigations into the molecular mechanisms linking vitamin D deficiency, NF- κ B activation, and placental immune responses may further clarify potential therapeutic targets and refine personalised strategies for preventing preterm labour.

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✦ CONFLICT OF INTEREST

None.

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Роль дефіциту вітаміну D у стимуляції запальної реакції та ризику передчасних пологів

Ірина Поладич

Кандидат медичних наук, доцент
Національний медичний університет імені О.О. Богомольця
01601, бульв. Тараса Шевченка, 13, м. Київ, Україна
<https://orcid.org/0000-0002-8494-2534>

Анотація. Передчасні пологи залишаються однією з провідних причин перинатальної смертності та довготривалої захворюваності новонароджених. Метою роботи було з'ясування ролі дефіциту вітаміну D у регуляції NF-κB-залежного прозапального каскаду у вагітних із передчасними пологами. У дослідженні були використані клініко-лабораторні, біохімічні та імунологічні методи, включно з визначенням рівня 25(OH)D, активності та фосфорильованих форм p65 NF-κB у плаценті, а також концентрацій TNF-α, IL-6 і CRP у сироватці крові. Було обстежено 114 вагітних жінок, які були розподілені на три групи: з передчасними пологами та дефіцитом вітаміну D (n = 44), з передчасними пологами та оптимальним рівнем вітаміну D (n = 40) та контрольну групу з фізіологічною вагітністю (n = 30). Було встановлено, що активність p65 NF-κB була найвищою у групі з дефіцитом вітаміну D – $59,21 \pm 0,24$ %, що перевищувало показники групи з оптимальним рівнем ($47,15 \pm 0,36$ %) та контролю ($28,46 \pm 0,37$ %) ($P < 0,05$). Концентрації TNF-α становили відповідно $42,75 \pm 0,31$, $30,44 \pm 0,29$ і $15,62 \pm 0,18$ пг/мл, IL-6 – $38,16 \pm 0,28$, $26,87 \pm 0,26$ та $12,44 \pm 0,14$ пг/мл, CRP – $6,82 \pm 0,12$, $4,31 \pm 0,09$ і $1,95 \pm 0,06$ мг/л ($P < 0,05$). Було підтверджено сильні кореляції між активністю NF-κB та рівнями TNF-α ($r = 0,88$), IL-6 ($r = 0,85$) і CRP ($r = 0,79$). Було узагальнено, що дефіцит вітаміну D асоціювався з гіперактивацією NF-κB та посиленням продукції прозапальних цитокінів, що сприяло розвитку передчасних пологів. Отримані результати можуть бути використані в акушерсько-гінекологічній практиці для стратифікації ризику передчасних пологів і розробки індивідуалізованих профілактичних заходів, спрямованих на корекцію вітамін-D статусу

Ключові слова: 25(OH)D; невиношування вагітності; NF-κB p65; запальні маркери; TNF-α; IL-6; плацента