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COMPARATIVE INDICATORS OF NON-SPECIFIC RESISTANCE FACTORS IN HEALTHY PREGNANT AND LACTATING WOMEN AND PREGNANT AND LACTATING WOMEN WITH PATHOLOGICAL CONDITIONS



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СОҒЛОМ ҲОМИЛАДОР ВА ЭМИЗИКЛИ АЁЛЛАР ҲАМДА ПАТОЛОГИК ҲОЛАТЛАРИ БЎЛГАН ҲОМИЛАДОР ВА ЭМИЗИКЛИ АЁЛЛАРДА НОСПЕЦИФИК РЕЗИСТЕНТЛИК ОМИЛЛАРИНИНГ ҚИЁСИЙ КЎРСАТКИЧЛАРИ

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СРАВНИТЕЛЬНЫЕ ПОКАЗАТЕЛИ ФАКТОРОВ НЕСПЕЦИФИЧЕСКОЙ РЕЗИСТЕНТНОСТИ У ЗДОРОВЫХ БЕРЕМЕННЫХ И КОРМЯЩИХ ЖЕНЩИН И У БЕРЕМЕННЫХ И КОРМЯЩИХ ЖЕНЩИН С ПАТОЛОГИЧЕСКИМИ СОСТОЯНИЯМИ

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Резюме. *Мақсад: қишлоқ жойларида доимий яшовчи соғлом ва патологик ҳолатлари бўлган ҳомиладор ва эмизикли аёллар қон зардобида комплемент тизимининг С3 компоненти (С3с), лактоферрин ва прокальцитонин концентрациясини қиёсий ўрганиш ҳамда диагностик ва прогностик мезонларни ишлаб чиқиш. Материал ва усуллар: Бухоро вилояти қишлоқ туманларида доимий яшовчи, ҳомиладорликнинг III триместрида ва лактация давридаги 19–49 ёшли 145 нафар аёлнинг қон зардоби иммунологик (ИФА), гематологик ва статистик усулларда текширилди. Натижалар: соматик патологияси (аутоиммун тиреоидит, турли даражадаги анемия) бўлган ҳомиладорларда (n=72) соғлом ҳомиладорларга (n=20) нисбатан С3с даражаси 1,23 марта (1,75±0,08 га қарши 1,42±0,04 мкг/мл; p<0,05), прокальцитонин 2,67 марта (0,16±0,03 га қарши 0,06±0,01 нг/мл; p<0,001) юқори, лактоферрин эса 1,31 марта паст (189,10±0,48 га қарши 247,15±0,88 мкг/мл; p<0,05) бўлди. Хулоса: С3с, лактоферрин ва прокальцитонин даражасининг ўзгариши соматик патология таъсирида иммун тизимининг зўриқишини ва бактериал транслокация туфайли антиген стимуляциясининг кучайишини акс эттиради; бу кўрсаткичларни ҳомиладорларнинг иммун ҳолатини баҳолашда дифференциал-диагностик ва прогностик мезон сифатида қўллаш тавсия этилади.*

Калит сўзлар: *комплемент, С3с компоненти, лактоферрин, прокальцитонин, носпецифик резистентлик, аутоиммун тиреоидит, ҳомиладорлик.*

Abstract. *Aim: to compare serum concentrations of complement component C3 (C3c), lactoferrin and procalcitonin as factors of non-specific resistance in healthy pregnant and lactating women and in those with pathological conditions permanently residing in rural areas, and to develop diagnostic and prognostic criteria. Materials and methods: blood serum of 145 women aged 19–49 years permanently residing in rural districts of the Bukhara region in the third trimester of pregnancy and during lactation was examined using immunological (ELISA), haematological and statistical methods. Results: in pregnant women with somatic pathology (autoimmune thyroiditis, anaemia of varying severity; n=72), compared with healthy pregnant women (n=20), C3c was 1.23-fold higher (1.75±0.08 vs 1.42±0.04 μg/mL; p<0.05) and procalcitonin 2.67-fold higher (0.16±0.03 vs 0.06±0.01 ng/mL; p<0.001), whereas lactoferrin was 1.31-fold lower (189.10±0.48 vs 247.15±0.88 μg/mL; p<0.05). Conclusion: changes in C3c, lactoferrin and procalcitonin reflect immune system strain under the influence of somatic pathology and increased antigenic stimulation due to bacterial translocation; these indicators are recommended as differential diagnostic and prognostic criteria for assessing the immune status of pregnant women.*

Keywords: *complement, C3c component, lactoferrin, procalcitonin, non-specific resistance, autoimmune thyroiditis, pregnancy.*

Current data indicate that cytokines, which participate both in regulating normal fetal development and in the complex mechanisms of pregnancy, may play a central regulatory role in many processes occurring in the fetoplacental complex. Interaction between trophoblast and decidual cells occurs through cytokines and their receptors, ensuring tolerance between the maternal organism and the fetus [5, 7, 10]. IL-4 regulates prostaglandin and cytokine production by monocytes, monocyte activation and T-cell cytotoxicity, whereas TGF-β regulates placental differentiation, trophoblast invasion and cytokine production by macrophages. IL-10 promotes the differentiation of Th0 cells towards the Th2 phenotype, inhibits the production of prostaglandins and cytokines by macrophages and enhances the expression of HLA-G molecules in trophoblast cells, which is necessary for successful implantation and maintenance of the Th2 profile [1, 2, 4, 12].

The reproductive function of the female body is particularly sensitive to environmental conditions and largely depends on the functional state of the immune system, which plays a central role in the adaptive response. Being an extremely complex, multicomponent system of rapidly dividing cells, the immune system is highly sensitive to anthropogenic factors and xenobiotics and can therefore serve as an indicator of an unfavourable ecological situation in a region; chemical, biological and physical factors induce adaptive changes in the immune system even in healthy individuals [3, 6, 8, 11].

Protecting the health of women of reproductive age permanently residing in rural districts who are in the third trimester of pregnancy or in the lactation period remains relevant, and early detection, diagnosis and prevention of pathological conditions arising during this period are among the pressing tasks of modern medicine. Although several studies have addressed this issue, they remain fragmented and lack a comprehensive approach; immune disorders in the «pregnant–postpartum–lactating woman» organism have not been studied comparatively, and diagnostic and prognostic criteria adapted to geographic living conditions have not been developed.

Aim of the study: to compare the serum concentrations of complement component C3 (C3c), lactoferrin and procalcitonin as factors of non-specific resistance in healthy pregnant and lactating women of reproductive age permanently residing in rural areas and in those with pathological conditions, and to develop diagnostic and prognostic criteria based on the results obtained.

Materials and methods. Blood and blood serum of 145 women of reproductive age (19–49 years) permanently residing in rural districts of the Bukhara region, in the third trimester of pregnancy and during lactation, were examined using immunological, haematological and statistical methods. The overall (pathological) group included 72 pregnant women with somatic pathology (autoimmune thyroiditis, anaemia of varying severity), and the comparison group included 20 healthy pregnant women. Serum C3c, lactoferrin and procalcitonin concentrations were determined by enzyme-linked immunosorbent assay (ELISA).

Results and discussion. Complement is a thermolabile system of serum β-globulin proteins that is normally inactive. It consists of nine components, is synthesised mainly by macrophages and hepatocytes and is activated by antigen–antibody complexes; two stages of complement activation (activation and cytolytic) and three activation pathways (classical, alternative and lectin) are distinguished [9]. Complement enhances the immune response, participates in the elimination of microorganisms and promotes clearance of immune complexes. However, excessive activation with production of the anaphylatoxins C3a and C5a may trigger septic processes, and activation within tissues (for example, at a site of necrosis) may contribute to autoimmune diseases and tissue destruction.

The C3 component was chosen for the study because it accounts for about 70% of the complement system and is its central component. In healthy pregnant women, the mean serum C3c level was 1.42±0.04 μg/mL, whereas in the overall (pathological) group it was significantly higher – 1.75±0.08 μg/mL, a 1.23-fold increase ($p<0.05$) (Table 1). We believe that this increase in women with autoimmune thyroiditis and anaemia indicates intensified activation processes, increased antigenic stimulation and an increased number of antigen–antibody complexes. In healthy pregnancy, partial activation of C3c is manifested by an increase in its serum level, whereas the presence of pathology is accompanied by disruption of component homeostasis. In our opinion, C3c may be used as a differential marker between healthy pregnancy and pregnancy complicated by somatic pathology and, in the latter, as a prognostic criterion of the outcome of these conditions.

Lactoferrin, a member of the transferrin family synthesised by epithelial cells of exocrine glands, is an iron-binding multifunctional protein that regulates iron content in the body, helps maintain the normal microflora, protects mucous membranes from pathogens and positively affects systemic and local immunity. As a factor of innate humoral immunity, it regulates the function of immunocompetent cells and is an acute-phase protein. In healthy pregnant women, the mean lactoferrin level was 247.15±0.88 μg/mL, whereas in the overall group with somatic diseases it was 189.10±0.48 μg/mL, i.e. 1.31-fold lower ($p<0.05$). This decrease in lactoferrin synthesis reflects strain of the immune system and has a negative effect on innate immunity.

Table 1. Non-specific resistance factors in healthy pregnant women and pregnant women with pathological conditions (M±m)

Group	C3c, μg/mL	Lactoferrin, μg/mL	Procalcitonin, ng/mL
Overall group (n=72)	1.75±0.08*↑	189.10±0.48*↓	0.16±0.03*↑
Healthy pregnant women (n=20)	1.42±0.04	247.15±0.88	0.06±0.01

*Note: ↑, ↓ – direction of change; * – statistically significant difference from healthy pregnant women.*

Procalcitonin is produced by thyroid parafollicular cells and neuroendocrine cells of the lungs and intestine in bacterial infections and tissue damage; as the precursor of calcitonin, it is also involved in calcium metabolism. In healthy individuals its serum level is low and rises mainly in bacterial inflammation. In healthy pregnant women, the serum procalcitonin concentration was 0.06±0.01 ng/mL, which is consistent with published data; the course of pregnancy did not affect this parameter. In pregnant women with somatic diseases, it was 2.67-fold higher – 0.16±0.03 ng/mL ($p<0.001$). Although these diseases are not bacterial, they affect the normal microflora: intestinal dysbiosis intensifies bacterial translocation from the intestine into the blood and parenchymal organs, to which the body responds with increased procalcitonin production (Fig. 1).

The ratio of the parameters between healthy women and women with somatic pathology was also calculated (Fig. 2). Thus, in pregnant women with somatic pathology, C3c and procalcitonin levels were significantly higher (1.23-fold and 2.67-fold, respectively) and the lactoferrin level was 1.31-fold lower than in healthy pregnant women ($p<0.05$–$p<0.001$).

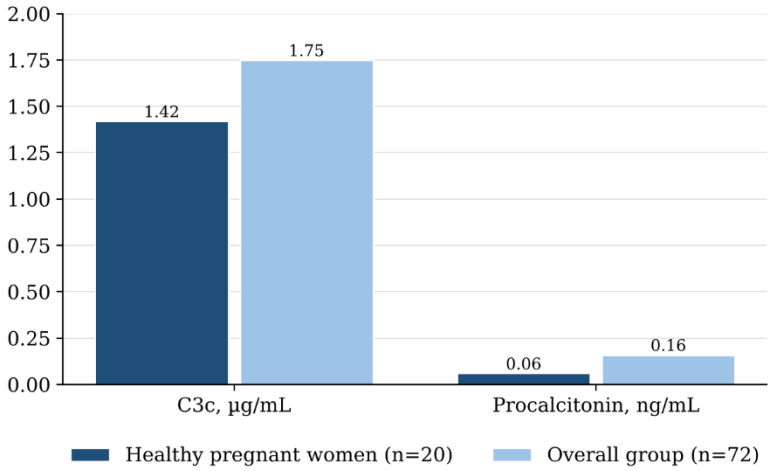


Fig. 1. Serum C3c (μg/mL) and procalcitonin (ng/mL) in healthy pregnant women and pregnant women with somatic pathology

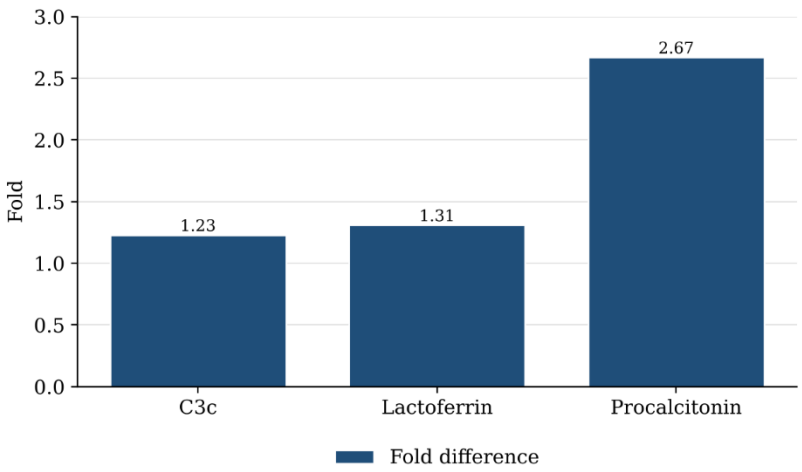


Fig. 2. Fold difference in non-specific resistance factors between pregnant women with somatic pathology and healthy pregnant women

We regard these changes as reflecting strain of the immune system under the influence of somatic pathology, increased antigenic stimulation due to bacterial translocation and the development of a pre-pathological condition.

Conclusions. Regular determination of serum C3c, lactoferrin and procalcitonin in healthy pregnant women and in pregnant women with pathological conditions is recommended for immunological monitoring, and the results may be used as differential diagnostic criteria of immune status and as prognostic criteria of pregnancy outcome.

Increased C3c and procalcitonin levels and decreased lactoferrin levels in pregnant women with somatic pathology (autoimmune thyroiditis, anaemia of varying severity) reflect strain of the immune system, increased antigenic stimulation due to bacterial translocation and the development of a pre-pathological condition, and may be used as a prognostic criterion.

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СРАВНИТЕЛЬНЫЕ ПОКАЗАТЕЛИ ФАКТОРОВ НЕСПЕЦИФИЧЕСКОЙ РЕЗИСТЕНТНОСТИ У ЗДОРОВЫХ БЕРЕМЕННЫХ И КОРМЯЩИХ ЖЕНЩИН И У БЕРЕМЕННЫХ И КОРМЯЩИХ ЖЕНЩИН С ПАТОЛОГИЧЕСКИМИ СОСТОЯНИЯМИ

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Резюме. *Цель: сравнительное изучение концентрации компонента С3 системы комплемента (С3с), лактоферрина и прокальцитонина в сыворотке крови здоровых беременных и кормящих женщин, постоянно проживающих в сельской местности, и женщин с патологическими состояниями, а также разработка диагностических и прогностических критериев. Материал и методы: иммунологическими (ИФА), гематологическими и статистическими методами исследована сыворотка крови 145 женщин 19–49 лет, постоянно проживающих в сельских районах Бухарской области, в III триместре беременности и в период лактации. Результаты: у беременных с соматической патологией (аутоиммунный тиреоидит, анемия различной степени; n=72) по сравнению со здоровыми беременными (n=20) уровень С3с был выше в 1,23 раза (1,75±0,08 против 1,42±0,04 мкг/мл; p<0,05), прокальцитонина – в 2,67 раза (0,16±0,03 против 0,06±0,01 нг/мл; p<0,001), а лактоферрина – ниже в 1,31 раза (189,10±0,48 против 247,15±0,88 мкг/мл; p<0,05). Выводы: изменения уровней С3с, лактоферрина и прокальцитонина отражают напряжение иммунной системы под влиянием соматической патологии и усиление антигенной стимуляции вследствие бактериальной транслокации; эти показатели рекомендуется использовать как дифференциально-диагностические и прогностические критерии иммунного статуса беременных.*

Ключевые слова: *комплемент, компонент С3с, лактоферрин, прокальцитонин, неспецифическая резистентность, аутоиммунный тиреоидит, беременность.*