ORIGINAL RESEARCH

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MEDICAL AND SOCIAL CHARACTERISTICS OF PREGNANT WOMEN WHO UNDERWENT COVID-19 AT THE PREGRAVIDAR STAGE

The pandemic of the new coronavirus infection COVID-19 (COVID-19) has had a significant impact on public health, including the reproductive health of women. There is little information on the impact of COVID-19, carried in the pregravidar period, on the course of pregnancy. The medical and social profile, somatic and reproductive health parameters of pregnant women who underwent COVID-19 at the pregravidar stage 6-12 months before pregnancy have not been studied. However, this information may be of significant importance for a preventive approach to the tactics of patient management at the stage of preparation for pregnancy and during gestation.

Keywords: medical and social profile, somatic pathology, new COVID-19 coronavirus infection, pregravidar stage.

Introduction. The COVID-19 pandemic has had a significant impact on the reproductive health of women [2, 7]. Direct infection with the SARS-CoV-2 virus, immune-mediated damage to the

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vascular endothelium, tissues of the bronchopulmonary system, heart, intestine, brain, liver and other organs leads to multisystem manifestations of COVID-19 and clinical polymorphism [1, 22]. With COVID-19, inflammasomes are activated, there is an increase in the levels of pro- and anti-inflammatory immunoregulatory cytokines [6, 23], and endothelial dysfunction develops. The latter leads to vasoconstriction, increased vascular permeability, impaired microcirculation, microthrombosis, hemorrhagic infarctions, necrosis and multiple organ disorders [16]. In pregnant women who have had COVID-19 during gestation, placental damage is formed, contributing to the development of placenta-associated complications [8, 14]. It is known that this infection leads to long-term consequences (post-COVID complications) in a number of patients, the development mechanisms of which are chronic systemic inflammation with an autoimmune component, endothelial dysfunction, thrombosis and hypoxia. Long-term consequences can be metabolic, cardiovascular, neurological disorders, decreased fertility [10, 11, 12, 17, 19, 21]. Information on the impact of COVID-19 suffered in the pregravid period on the course of pregnancy is scarce. Thus, in the study by N.A. Frankevich [13] it was shown that patients who had recovered from the disease at the pregravid stage had worse obstetric and perinatal outcomes, in particular, if pregnancy occurred less than two months after COVID-19, a decrease in the frequency of live births was

observed, which is possibly due to a large proportion of low-quality embryos. In patients with a severe form of the disease, the risk of pregnancy loss before 12 weeks increased by 5 times, and the risk of late preeclampsia - by 7.7 times, which can affect perinatal outcomes. In this regard, patients are advised to postpone pregnancy planning for 2-6 months in order to minimize the risk of obstetric complications. At the same time, the medical and social profile, the features of the somatic and reproductive health of patients who have had COVID-19, planning pregnancy within 6-12 months after COVID-19 have not been studied. At the same time, knowledge and analysis of the data of the medical and social profile, somatic and reproductive health of patients will substantiate the approach to the tactics of patient management at the stage of preparation for pregnancy and during gestation.

Aim: to determine the medical and social portrait, parameters of somatic and reproductive health of pregnant women who had COVID-19 at the pre-pregnancy stage 6-12 months before pregnancy.

Materials and methods. A retrospective cohort study of 265 pregnant women observed in 2021-2024 at the State Autonomous Healthcare Institution "Regional Clinical Hospital No. 3" in Chelyabinsk was conducted. An analysis of medical documentation was carried out: individual medical records of pregnant women and women in labor, birth histories, medical records of patients receiving medical care on an outpatient basis. Medical

and social characteristics, the state of somatic and reproductive health were studied. The study was approved by the Ethics Committee of the Federal State Budgetary Educational Institution of Higher Education "South Ural State Medical University" of the Ministry of Health of the Russian Federation. The main group consisted of 152 patients who had COVID-19 in the pregravid period 6 to 12 months before pregnancy; the comparison group included 113 women who did not have COVID-19 during the pandemic and were not vaccinated against COVID-19. Inclusion criteria for the main group: documented fact of COVID-19 (U07.1) 6 to 12 months before pregnancy, availability and accessibility of medical records, observation at a antenatal clinic, reproductive age. Exclusion criteria: probable / suspected case of COVID-19 (U07.2/Z03.8), lack or inaccessibility of medical records, multiple pregnancy, HIV infection, psychiatric diseases, somatic pathology in the decompensation stage, malignant tumors. Inclusion criteria for the comparison group: no history of confirmed, probable, or suspicious COVID-19, observation at a women's clinic, reproductive age, availability and accessibility of medical documentation. Exclusion criteria: severe extragenital pathology in the decompensation stage, oncopathology, HIV infection, psychiatric illness, multiple pregnancy.

The severity of COVID-19 suffered by the patient was assessed based on the document of the Ministry of Health of the Russian Federation - "Temporary guidelines "Prevention, diagnosis and treatment of a new coronavirus infection (COVID-19). Version 18 (26.10.2023)".

Statistical analysis of the study results was carried out using Microsoft Excel 2016 spreadsheets. The characteristics of qualitative indicators are presented as absolute numbers and relative values in percent. Statistically significant differences in proportions were determined using the z-test. The normality of the distribution was assessed based on the Pearson test. Quantitative features of the estimated values that obey the normal distribution law are presented as the mean value (M) and standard deviation (m). Statistically significant differences were assessed using the Student t-test. The critical level of significance was taken as p=0.05.

Results and discussion. Patients of the main group had acute COVID-19 6-12 months before pregnancy: mild form – 98 / 152 (64.5%), moderate form – 42 / 152 (27.6%), severe form – 12 / 152 (7.9%). At the same time, COVID-asso-

ciated pneumonia was observed in 21 / 152 (13.8%) women, of which 18 (85.7%) received in-hospital treatment according to temporary guidelines that were relevant at the time of supervision.

The age of patients in both groups corresponded to early reproductive age: in the main group, the average age was 32.2±0.63, in the comparison group - 31.5±0.71, which did not have statistically significant differences. In both groups, women belonged predominantly to the East Slavic ethnic group, which prevailed in the main group: 135 / 152 (88.8%) and 86 / 113 (76.1%) (p=0.01). Most patients in both groups lived in the Chelyabinsk region: in the main group – 105 / 152 (69.1%), in the comparison group – 87 / 113 (77.0%) (p=0.15), in the city of Chelyabinsk – 47 / 152 (30.9%) and 26 / 113 (23.0%) (p=0.15), respectively. A total of 74 / 152 (48.7%) patients in group 1 and 42 / 113 (37.2%) patients in group 2 had higher education (p=0.06), incomplete higher education – 4 / 152 (2.6%) and 2 / 113 (1.8%) – respectively in the groups (p=0.64), secondary general education – 28 / 152 (18.4%) and 49 / 113 (43.4%) (p=0.001), secondary specialized education – 46 / 152 (30.3%) and 20 / 113 (43.4%) (p=0.02). In the main group, the employed made up 110 / 152 (72.4%), in the 2nd group – 75 / 113 (66.4%) (p=0.29), housewives 41 / 152 (27.0%) and 37 / 113 (32.7%) (p=0.31), students – 1 / 152 (0.7%) and 1 / 113 (0.9%) (p=0.83), respectively. 122 / 152 (80.3%) and 97 / 113 (85.8%) pregnant women were in registered marriage, respectively (p=0.24). Thus, the patients of both groups did not have statistically significant differences in place of residence, education, social status and family relationships. Among the bad habits, only smoking was noted in patients of both groups: in the main group – 13 / 152 (8.6%), in the comparison group – 3 / 113 (2.7%) (p=0.05).

All patients in the main group had an aggravated somatic history, while in the comparison group, chronic somatic pathology was not detected in 46 / 113 (40.7%). Hypertension was observed with almost equal frequency in both groups – 20 / 152 (13.6%) and 12 / 113 (10.6%) (p=0.53), diseases of the genitourinary system – 14 / 152 (9.2%) and 9 / 113 (7.9%) (p=0.72), chronic anemia – 6 / 152 (3.9%) and 2 / 113 (1.8%) (p=0.31), diseases of the respiratory system – 20 / 152 (13.2%) and 8 / 113 (7.1%) (p=0.11). Despite the absence of a statistically significant difference, it should be noted that respiratory diseases were registered twice as often after COVID-19. It is note-

worthy that lipid metabolism disorders of varying degrees were present in 38.2% of women in the main group and 37.2% of patients in the comparison group. At the same time, obesity of varying degrees was statistically significantly more common in the main group: 47 / 152 (30.9%) and 19 / 113 (16.8%) (p=0.01). Moreover, 40 / 47 (85.1%) obese patients in the main group noted a progressive increase in body weight after COVID-19. This may be due to a stressful situation, forced social isolation, and physical inactivity during the quarantine and anti-epidemic measures. According to literary data, a change in body weight as a manifestation of post-COVID syndrome can occur in 10.6 – 20% of patients [20].

In 8 / 152 (5.3%) patients, type 2 diabetes mellitus was diagnosed for the first time in the post-COVID period; diabetes mellitus was not registered in the comparison group (p=0.01). It is known that the risk of developing diabetes mellitus in the post-COVID period is 59% higher [15]. Impaired carbohydrate metabolism in the post-COVID period may be due to the direct damaging effect of SARS-CoV-2 on pancreatic β-cells, increased insulin resistance against the background of acute COVID-19, and the influence of pathogenetically justified glucocorticosteroid therapy [5].

With COVID-19 and Long-COVID infection, the state of the intestinal microbiome is disrupted, diarrhea, abdominal pain, constipation, nausea, heartburn, belching may occur [4]. In our study, gastrointestinal diseases were statistically significantly more often detected in patients in the main group – 46 / 152 (30.3%) versus 18 / 113 (15.9%) in the comparison group (p = 0.01). Moreover, irritable bowel syndrome, functional dyspepsia, intestinal dysbiosis were registered in the post-COVID period in 27 / 46 (58.7%).

It is currently known that the SARS-CoV-2 virus provokes the development of thyroid pathologies (subacute thyroiditis, diffuse toxic goiter, euthyroid sick syndrome, chronic thyroiditis with thyroid dysfunction) [3]. Our studies have shown that thyroid diseases (hypothyroidism, hyperthyroidism, autoimmune thyroiditis, non-toxic diffuse goiter) were statistically significantly more often detected in patients of the main group: 25 / 152 (16.5%) versus 7 / 113 (6.2%) (p=0.01). At the same time, during pre-pregnancy preparation, thyroid diseases were detected in 19 / 25 (76.0%) in the post-COVID period.

Ophthalmological manifestations of COVID-19 have been described both in

the acute stage of infection and in the post-COVID period. Such lesions as conjunctivitis, uveitis, retinal microangiopathy, central retinal vein thrombosis, and others are encountered [9]. In our material, eye diseases were statistically significantly more common in patients in the main group than in the comparison group: 64 / 152 (42.1%) and 30 / 113 (26.6%), respectively (p=0.01). In addition to refractive and accommodation disorders, which prevailed in the comparison group, conjunctivitis, scleritis, episcleritis, and uveitis were detected in patients in the post-COVID period.

According to the obstetric history indicators, the patients did not have statistically significant differences, in particular, 52 / 152 (34.2%) and 32 / 113 (28.3%) were primiparous (p=0.31); 23 / 152 (15.1%) and 20 / 113 (17.7%) were multiparous primiparous (p=0.58), and 77 / 152 (50.7%) and 61 / 113 (53.9%) were multiparous (p=0.59). Abortion at the woman's request (surgical or medical) was in the history of 29 / 152 (19.1%) patients in the main group and 27 / 113 (23.9%) patients in the comparison group (p=0.34). The frequency of spontaneous abortion (including non-viable pregnancy) was 21 / 152 (13.8%) and 17 / 113 (15.0%) (p=0.09) respectively in the groups.

Gynecological diseases in the anamnesis were diagnosed in women of both groups almost identically, except for the violation of the vaginal microbiocenosis. Thus, uterine fibroids were registered in 19 / 152 (12.5%) patients of the main group and 7 / 113 (6.2%) of the comparison group (p=0.09); inflammatory diseases of the female pelvic organs in 27 / 152 (17.8%) and 14 / 113 (12.4%) (p=0.31); polycystic ovary syndrome in 6 / 152 (3.9%) and 3 / 113 (2.7%) (p=0.57); menstrual cycle disorders - in 3 / 152 (1.9%) and 2 / 113 (1.8%) (p=0.90); endometriosis - in 3 / 152 (1.9%) and 0 / 113 (0.0%) (p=0.13); respectively, in the groups. Bacterial vaginosis was detected in 28 / 152 (18.4%) patients in the main group and 11 / 113 (9.7%) in the comparison group (p=0.05). The latter circumstance is expected in the post-COVID period, including in connection with the disruption of the intestinal microbiota, which was recorded in our material and is consistent with literary data [18, 24].

Conclusion. Thus, pregnant women who had COVID-19 at the pre-gravid stage 6-12 months before pregnancy have a number of features of the medical and social portrait, somatic and reproductive health, in particular, there is a higher frequency of smoking, comorbid somatic pathology (obesity, diabetes mellitus, diseases of the gastrointestinal tract, thyroid gland and organs of vision) and bacterial vaginosis. Moreover, the above-described pathology often occurs for the first time, as a consequence of COVID-19, and can be a significant predictor of complicated pregnancy. It is advisable to take into account the data obtained by us when conducting pre-gravid preparation in patients who have had COVID-19.

The authors declare no conflict of interest in the submitted article.

References

1. Voropaeva E.E., et al. Kliniko-laboratornye osobennosti i materinskie iskhody u beremennyh s kriticheskim porazheniem legkih pri COVID-19 [Clinical and laboratory features and maternal outcomes in pregnant women with critical lung damage in the COVID-19]. Ural'skij medicinskij zhurnal [Ural Medical Journal. 2024; Vol.23, No. 1: 90-103. DOI: 10.52420/2071-5943-2024-23-1-90-103 (In Russ.).]

2. Chazova I.E., et al. Konsensus ekspertov Rossijskogo medicinskogo obshchestva po arterial'noj gipertonii: arterial'naya gipertoniya i postkovidnyj sindrom [Russian medical society expert consensus on arterial hypertension: arterial hypertension and post-COVID syndrome]. Sistemnye gipertenzii [Systemic Hypertension. 2022; Vol.19, No 3: 5-13. DOI: 10.38109/2075-082X-2022-3-5-13 (In Russ.).]

3. Maksim O.V., Romashevsky B.V., Demyanenko N.Yu. Osobennosti patogeneza zabolevanij shchitovidnoj zhelezy pri COVID-19 [Features of the pathogenesis of thyroid diseases in COVID-19]. Farmateka [Farmateka. 2023; No. 3: 34-43. DOI: 10.18565/pharmateca.2023.3.34-43 (In Russ.).]

4. Metodicheskie rekomendacii «Osobennosti techeniya Long-COVID-infekcii. Terapevticheskie i reabilitacionnye meropriyatiya» [Methodological recommendations "Features of Long-COVID infection clinical course. Therapeutic and rehabilitation measures"]. Terapiya [Therapy. 2022; Vol.8, No. S1: 1-147. DOI: 10.18565/therapy.2022.1suppl.1-147 (In Russ.).]

5. Karonova T.L., et al. Narusheniya uglevodnogo obmena, associirovannye s COVID-19: kliniko-morfologicheskoe issledovanie [Glucose metabolism disorders associated with COVID-19: clinical and morphological study]. Saharnyj diabet [Diabetes Mellitus. 2023; Vol.26, No. 6: 515-525. DOI: 10.14341/DM13041 (In Russ.).]

6. Nasonov E.L. Koronavirusnaya bolezn' 2019 (COVID-19) i autoimmunitet [Coronavirus disease 2019 (COVID-19) and autoimmunity]. Nauchno-prakticheskaya revmatologiya [Rheumatology Science and Practice. 2021. Vol.59, No. 1. P. 5-30. DOI: 10.47360/1995-4484-2021-5-30] (In Russ.).

7. Ishchenko L.S., et al. Novaya koronavirusnaya infekciya COVID-19 i reproduktivnoe zdorov'e zhenshchin. Fakty i predpolozheniya [New coronavirus infection COVID-19 and women's reproductive health. Facts and assumptions]. Yakutskij medicinskij zhurnal [Yakut Medical Journal. 2022; No. 2(78): 96-101. DOI: 10.25789/YMJ.2022.77.25 (In Russ.).]

8. Voropaeva E.E., et al. Perinatal'nye iskhody i rezul'taty morfologicheskogo issledovaniya placent u beremennyh s kriticheskim porazheniem legkih pri novoj koronavirusnoj infekcii COVID-19 [Perinatal outcomes and morphological examination of placentas in pregnant women with critical lung lesions in new COVID-19 coronavirus infection]. Ural'skij medicinskij zhurnal [Ural Medical Journal. 2023; Vol.22, No. 2: 109-121. DOI: 10.52420/2071-5943-2023-22-2-109-121 (In Russ.).]

9. Belyaeva A.I., et al. Postkovidnye oftal'mologicheskie proyavleniya na zadnem otrezke glaza [Postcovid ophthalmic manifwstations in the posterior segment of the eye]. Sovremennye problemy nauki i obrazovaniya [Modern problems of science and education. 2023; №1. URL: https://science-education.ru/ru/article/view?id=32391 DOI: 10.17513/spno.32391 (In Russ.).]

10. Adamyan L.V., et al. Postkovidnyj sindrom v akusherstve i reproduktivnoj medicine [Post-COVID-19 syndrome in obstetrics and reproductive medicine]. Problemy reprodukcii [Russian Journal of Human Reproduction. 2021; Vol. 27, No.6: 30-40. DOI: 10.17116/repro20212706130 (In Russ.).]

11. Belokrinitskaya T.E., et al. Postkovidnyj sindrom u beremennyh [Postcovid syndrome in pregnant women]. Akusherstvo i ginekologiya [Obstetrics and Gynecology. 2023; No. 6: 60-68. DOI: 10.18565/aig.2023.54 (In Russ.).]

12. Karateev A.E., et al. «Postkovidnyj sindrom»: v centre vnimaniya skeletno-myshechnaya bol' ["Post-COVID syndrome": the focus is on musculoskeletal pain]. Nauchno-prakticheskaya revmatologiya [Rheumatology Science and Practice. 2021; Vol.59, No. 3: 255-262. DOI: 10.47360/1995-4484-2021-255-262 (In Russ.).]

13. Frankevich N.A. Profilaktika oslozhnenij beremennosti pri COVID-19 na osnovanii differencirovannogo podhoda k pregravidarnoj podgotovke, vedeniyu beremennosti i rodov: special'nost' 3.1.4 «Akusherstvo i ginekologiya»: avtoref. dis. … d-ra med. nauk. Moskva, 2024: 46. [Prevention of pregnancy complications in COVID-19 based on a differentiated approach to pre-pregnancy preparation, management of pregnancy and childbirth: specialty 3.1.4 "Obstetrics and gynecology": abstract of the dissertation. ... Doctor of Medical Sciences. Moscow, 2024. 46 p. (In Russ.).]

14. Shchegolev A.I., Tumanova U.N., Serov V.N. Porazheniya placenty u beremennyh s SARS-CoV-2-infekciej [Placental lesions in pregnant women with SARS-COV-2 infection]. Akusherstvo i ginekologiya [Obstetrics and Gynecology. 2020; No. 12:44-52. DOI: 10.18565/aig.2020.12.44-52.] (In Russ.).

15. Banerjee M., Pal R., Dutta S. Risk of incident diabetes post-COVID-19: A systematic review and Meta-analysis. Prim Care Diabetes. 2022; 16: 591-593. DOI: 10.1016/j.Pcd.2022.05.009.

16. Varga Z., et al. Endothelial cell infection and endotheliitis in COVID-19. Lancet. 2020; 395(10234): 1417-1418. DOI: 10.1016/S0140-6736(20)30937-5.

17. Haffke M., et al. Endothelial dysfunction and altered endothelial biomarkers in patients with post-COVID-19 syndrome and chronic fatigue syndrome (ME/CFS) / // J Transl Med. 2022; 20(1): 138. DOI: 10.1186/s12967-022-03346-2.

18. Gut microbiota composition reflects disease severity and dysfunctional immune responses in patients with COVID-19 / Y. Yeoh [et al.] // Gut. 2021; 70(4): 698-706.

19. Long term Cardiovascular Manifestations and Complications of COVID-19: Spectrum and Approach to Diagnosis and Management / V. Khetpal [et al.] // R Med Z (2013). 2022; 105(7): 16-22.