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Features of the Course of Pregnancy Complicated by Gestational Diabetes and a Novel Coronavirus Infection

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ABSTRACT

Aim. To study the role of metabolic disorders in the development of perinatal complications of the novel coronavirus infection.

Materials and methods. The analysis of the course of pregnancy and childbirth in pregnant women who had a novel coronavirus infection (170) and without it (100), and their newborns (270).

Results. A novel coronavirus infection (NCI) during pregnancy leads to the development of complications: preeclampsia ($p = 0.012$), premature birth ($p = 0.038$), premature detachment of the normally located placenta ($p = 0.05$), fetal growth retardation ($p = 0.028$), gestational diabetes mellitus (GDM) ($p = 0.023$), intrauterine infection ($p = 0.048$) and asphyxia of the newborn ($p = 0.04$). Gestational diabetes mellitus is 2 times more likely to accompany a moderate form of NCI, as opposed to a mild one ($p = 0.001$). Infection with the SARS-CoV2 virus on the background of previous GDM contributes to the development of moderate NCI ($p = 0.005$). Hyperglycemia in GDM after moderate NCI more often than after mild requires the appointment of insulin ($p = 0.03$). The combination of NCI and GDM is characterized by the development of polyhydramnios ($p = 0.02$), the risk of which increases in the presence of hereditary thrombophilia. The neonatal period is more often complicated by intrauterine pneumonia if the mother has a combination of NCI and GDM.

Conclusion. The risk of developing metabolic disorders and perinatal complications in pregnant women who had a novel coronavirus infection is significantly higher than in pregnant women without a novel coronavirus infection.

Keywords: COVID-19, pregnancy, gestational diabetes mellitus, polyhydramnios

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Особенности течения беременности, осложненной гестационным диабетом и перенесенной новой коронавирусной инфекцией

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РЕЗЮМЕ

Цель. Изучение влияния новой коронавирусной инфекции на развитие метаболических нарушений и перинатальных осложнений.

Материалы и методы. Проведен анализ течения беременности и родов у беременных, перенесших новую коронавирусную инфекцию (170) и без таковой (100), и анализ историй их новорожденных (270).

Результаты. Новая коронавирусная инфекция (НКИ), перенесенная во время беременности, приводит к развитию осложнений: преэклампсии ($p = 0,012$), преждевременным родам ($p = 0,038$), преждевременной отслойке нормально расположенной плаценты ($p = 0,05$), недостаточному росту плода ($p = 0,028$), гестационному сахарному диабету (ГСД) ($p = 0,023$), внутриутробной инфекции ($p = 0,048$) и асфиксии новорожденного ($p = 0,04$). Гестационный сахарный диабет в 2 раза чаще сопровождает среднетяжелую форму НКИ в отличие от легкой ($p = 0,001$). Инфицирование вирусом SARS-CoV2 на фоне предшествующего ГСД способствует развитию среднетяжелой степени НКИ ($p = 0,005$). Гипергликемия при ГСД после перенесенной среднетяжелой НКИ чаще, чем после легкой, требует назначения инсулина ($p = 0,03$). Для сочетания НКИ и ГСД характерно развитие многоводия ($p = 0,02$), риск которого возрастает при наличии наследственной тромбофилии. Период новорожденности чаще осложняется внутриутробной пневмонией при наличии у матери сочетания НКИ и ГСД.

Заключение. Риск развития метаболических нарушений и перинатальных осложнений у беременных, перенесших новую коронавирусную инфекцию, значимо выше по сравнению с беременными без новой коронавирусной инфекции.

Ключевые слова: COVID-19, беременность, гестационный сахарный диабет, многоводие

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INTRODUCTION

Analyses of the consequences of the novel coronavirus infection (NCI) pandemic have demonstrated the multisystem nature of vital organ damage. As early as 2003, during the predominance of atypical viral

pneumonia caused by SARS-CoV coronavirus, studies demonstrated the expression of angiotensin-converting enzyme receptor type 2 (ACE2) in bronchi, adipose tissue, skeletal muscle, lung parenchyma, ileum, cardiovascular tissues, kidneys, liver, gastrointestinal tract, and pancreas [1, 2]. The cases of type 1 diabetes

mellitus identified at that time demonstrated the direct impact of the coronavirus family on endocrine organs [3]. The significant increase in gestational diabetes mellitus (GDM) incidence during the NCI pandemic is likely due to a similar pathogenesis. The problem of increased metabolic disorders in pregnant women with novel coronavirus infection is relevant due to GDM's significant contribution to maternal and neonatal complications.

The aim of this study was to investigate the impact of novel coronavirus infection on the development of metabolic disorders and perinatal complications.

MATERIALS AND METHODS

A comparative analysis of 270 pregnancy, delivery, and neonatal histories was performed from January to December 2021. Based on novel coronavirus infection status during pregnancy, patients were divided into two groups: the study group consisted of 170 women with NCI, and the control group included 100 patients without NCI.

Comparison of anthropometric, demographic, and anamnestic data between the clinical groups showed statistical comparability for the main parameters (Tables 1.1–1.3).

Table 1.1

Age of Subjects, $Me (Q_1; Q_3)$ [25-75 %]			
Parameter	Clinical groups		p
	study ($n = 170$)	control ($n = 100$)	
Age, years, $Me (Q_1; Q_3)$	31 (28; 36)	31 (26; 36)	0.90

Note. The Mann–Whitney test was used to calculate the significance level of p .

Table 1.2

Obstetric and Gynaecological History, n (%)			
Parameter	Clinical groups		p
	study ($n = 170$)	control ($n = 100$)	
First-time pregnant women, n (%)	28 (16.5)	26 (26)	0.059
Recurrent pregnancies, n (%)	142 (83.5)	74 (74)	0.059
First-born women, n (%)	62 (36.4)	32 (32)	0.45
Repeat births, n (%)	108 (63.6)	68 (68)	0.45
Abortion, n (%)	54 (31.7)	29 (29)	0.63
Miscarriage, n (%)	50 (29.4)	25 (25)	0.43
Ectopic pregnancy, n (%)	24 (14.1)	12 (12)	0.62

Note. The χ^2 criterion with Yates correction was used to calculate the significance level of p .

The inclusion criteria for the study were as follows: absence of severe extragenital pathology, including severe forms of type 1 and type 2 diabetes mellitus (DM); absence of HIV infection; absence of fetal

malformations; singleton pregnancy; and the patient's informed consent to participate in the study.

Table 1.3

Structure of Extragenital Diseases, n (%)			
Parameter	Clinical groups		p
	study ($n = 170$)	control ($n = 100$)	
Arterial hypertension, n (%)	17 (10)	10 (10)	1.0
Type 2 diabetes mellitus, n (%)	4 (2.3)	2 (2)	0.85
Anemia, n (%)	95 (55.8)	57 (57)	0.86
Obesity, n (%)	31 (18.2)	23 (23)	0.345

Note. The χ^2 criterion with Yates correction was used to calculate the significance level of p .

Treatment of novel coronavirus infection (NCI) during pregnancy was conducted in respiratory hospitals at the Tomsk Medical Center No. 2 and the Tomsk Maternity Hospital No. 4. Delivery and subsequent examination of the patients were performed at the Tomsk Regional Perinatal Center named after I.D. Yevtushenko.

Upon admission to the regional perinatal center, patients underwent a standard examination as outlined in clinical protocols. Diagnostic procedures included ultrasound and Doppler ultrasonography using Nemio XG equipment (Toshiba, Japan). During labor, cardiotocography (CTG) monitoring was conducted with Sonicaid Team devices (Sonicaid Ltd/Huntleigh Healthcare, UK) and FC 1400 systems (Bionet, South Korea).

Fibrinogen is a significant modulator of coagulation and inflammatory processes [4], so patients from both groups were examined for hereditary thrombophilia, including the fibrinogen (FGB) gene polymorphism (examination was conducted using kits manufactured by DNA Technology LLC, Russia).

The results of the study were processed via the variational statistics method using the Statistica 12 application software package. Absolute and relative frequencies were used to describe qualitative data. The χ^2 criterion with Yates correction, n (%) was used to compare qualitative data. The Mann–Whitney test was used to compare nonparametric quantitative data from the two groups. The results are presented in the form of the median and the interquartile range $Me (Q_1; Q_3)$. The significance level is $p < 0.05$.

RESULTS

The course of pregnancy and delivery in women who experienced novel coronavirus infection (NCI), in contrast to uninfected women, was complicated

in 16.5% of cases (28/170) versus 5% (5/100) in the control group by preterm labor ($p = 0.038$). In 7.7% (13/170) of patients (versus 2% (2/100) in the control group), pregnancy was complicated by premature detachment of the normally located placenta ($p = 0.05$). Pre-eclampsia (PE) occurred in 16.5% (28/170) versus 5% (5/100) in the control group ($p = 0.012$). Gestational diabetes mellitus (GDM) developed in 39% (64/170) of pregnant women versus 24% (24/100) in the control group ($p = 0.023$).

The frequency of insulin prescriptions had no significant differences between the groups, regardless of NCI status ($p = 0.7$). In the study group, GDM was diagnosed twice as often after NCI infection rather than preceding it. There is a dependence of insulin prescription in GDM on the time of NCI infection — developing before NCI, GDM in the study group more often required insulin therapy (Table 2).

Table 2

Dependence of Insulin Prescription in GDM on the Time of NCI Infection, n (%)			
Parameter	GDM (64 in total)		p
	GDM before NCI (21)	GDM after NCI (43)	
Insulin prescription for correction (%)	8 (38)	5 (12)	0.014
Diet correction (%)	13 (62)	38 (88)	

Note. The χ^2 criterion with Yates correction was used to calculate the significance level of p .

The correlation between the severity of NCI and the probability of complications in our study was found only for the moderately severe form of NCI and GDM (Table 3).

Table 3

Gestational Complications Depending on the Severity of Novel Coronavirus Infection, n (%)			
Parameter (number of cases)	Mild NCI $n = 131$	Moderately severe NCI $n = 39$	p
Preeclampsia (28)	19 (14.5)	9 (23)	0.2
Premature detachment of the normally located placenta (13)	10 (7.6)	3 (7.7)	0.8
Fetal growth retardation (35)	28 (21.3)	7 (17.9)	0.6
Premature birth (25)	19 (14.5)	6 (15.3)	0.89
Gestational DM (64)	41 (31.3)	24 (61.5)	0.001

Note. The χ^2 criterion with Yates correction was used to calculate the significance level of p .

Additionally, a moderately severe degree of NCI developed significantly more often if the patient already had GDM at the time of SARS-CoV 2 infection (Table 4).

Table 4

Dependence of the Severity of Novel Coronavirus Infection on the Presence of Gestational DM Before Infection, n (%)		
Parameter	Study group ($n = 170$)	
	Mild, 131 (77)	Moderately severe, 39 (23)
GDM before NCI ($n = 21$)	11 (8.4)	10 (25.6)
No GDM before NCI ($n = 149$)	120 (91.6)	29 (74.4)

Note. The χ^2 criterion with Yates correction was used to calculate the significance level of p .

Insulin administration for the correction of hyperglycemia in GDM in our study was required more frequently after moderate NCI than after mild NCI ($p = 0.03$).

Changes in the amount of amniotic fluid are pathognomonic for both intrauterine infection (IUI) and GDM. In the group of pregnant women who developed polyhydramnios, the formation of this complication was found to be dependent on NCI. In the control group, there was no correlation between the development of polyhydramnios and the presence of GDM (Table 5).

Table 5

Dependence of the Presence of Polyhydramnios in Gestational Diabetes Mellitus on the Novel Coronavirus Infection, n (%)		
Parameter	Study group ($n = 170$)	
	Gestational DM ($n = 64$)	Normoglycaemia ($n = 106$)
Polyhydramnios, ($n = 24$)	14 (21.8)	10 (9.9)
Parameter	Control group ($n = 100$)	
	Gestational DM ($n = 38$)	Normoglycaemia ($n = 62$)
Polyhydramnios, ($n = 11$)	4 (10.5)	7 (11.2)

Note. The χ^2 criterion with Yates' correction was used to calculate the significance level of p .

When analysing the possible factors for the development of polyhydramnios (fetal abnormalities, multiple pregnancies, GDM), we found a dependence of the increased amount of amniotic fluid on the presence of fibrinogen gene polymorphism. Polyhydramnios is significantly more likely to develop after an NCI in the presence of a homozygous carrier of the A allele in the FGB-455 fibrinogen gene (Table 6).

We can assume that there is a negative synergy of infectious and dysmetabolic processes in the formation of polyhydramnios. The outcome of the latter is usually premature birth, fetal distress, and asphyxia during labour.

Table 6

Dependence of the Presence of Polyhydramnios in Novel Coronavirus Infection on the Presence of a Polymorphic Variant of the Fibrinogen Gene, <i>n</i> (%)			
FGB 455 genotype	Study group (<i>n</i> = 170)		<i>p</i>
	Polyhydramnios (<i>n</i> = 24)	Normohydramnios (<i>n</i> = 146)	
FGB 455 G/A, G/G (<i>n</i> = 160)	19 (79)	141 (96)	0.0034
FGB 455 A/A (<i>n</i> = 10)	5 (21)	5 (4)	

Note. The χ^2 criterion with Yates' correction was used to calculate the significance level of *p*.

Analysis of perinatal complications in both groups showed that 20.6% of patients in the study group (35/170) (compared to 9% (9/100) in the control group) were diagnosed with fetal growth retardation ($p = 0.028$). Additionally, antenatal fetal death was recorded in 3% of patients in the study group (5/170) (compared to 1% (1/100) in the control group) ($p = 0.56$).

The Apgar score at 1 minute in newborns from mothers who had suffered from NCI was significantly lower than in the control group. No statistically significant difference was found when comparing anthropometric indicators of newborns in both groups (Table 7).

Table 7

Newborns' Records, <i>Me</i> , <i>Q</i> ₁ - <i>Q</i> ₃ [25-75%]			
Parameter	Clinical groups		<i>p</i>
	Study group (<i>n</i> = 170)	Control group (<i>n</i> = 100)	
Height, cm	53 (50; 55)	53 (51; 55)	0.90
Weight, kg	3,320 (2,997.5; 3,702.5)	3,340 (3,025; 3,635)	0.65
Apgar score at 1 min, points	8 (8.5; 9)	9 (9; 9)	0.004
Apgar score at 5 min, points	8 (8; 9)	9 (9; 9)	0.6

Note. The Mann-Whitney test was used to calculate the significance level of *p*.

When analysing the condition of newborns, changes characteristic of both the entire study group and the combination of NCI and GDM were revealed. Asphyxia during labour was diagnosed in 10% of newborns from mothers with NCI (OR 3.59, $p = 0.04$). 14% (24/170) (compared to 5% (5/100) in the control group) of newborns from the study group required transfer to the Intensive Care Unit of the Neonatal Pathology Department ($p = 0.02$). However, there were no significant differences between the groups in the incidence of complications of neonatal adaptation,

such as hypoglycaemia, wet lung syndrome, supraphysiological weight loss, and early jaundice up to 2 days.

In the study of neonatal complications in the main group, the negative contribution of maternal GDM to the development of intrauterine infection was confirmed (Table 8).

Table 8

Comparative Characteristics of Neonatal outcomes After NCI During Pregnancy Depending on the Presence of GDM, <i>n</i> (%)			
Parameter	Study group (<i>n</i> = 170)		<i>p</i>
	GDM (<i>n</i> = 64)	No GDM (<i>n</i> = 106)	
- fetal growth retardation, <i>n</i> (%)	6 (9.3)	13 (12.2)	0.5
- fetal macrosomia, <i>n</i> (%)	4 (6.2)	6 (5.6)	0.5
- birth asphyxia, <i>n</i> (%)	2 (3.1)	6 (5.6)	0.45
- unspecified IUI, <i>n</i> (%)	4 (6.2)	1 (0.9)	0.048

Note. The χ^2 criterion with Yates correction was used to calculate the significance level of *p*.

The "unspecified intrauterine infection: pneumonia of unspecified aetiology" diagnosis was slightly more common in women in the study group with concomitant GDM ($p = 0.048$). SARS-CoV-2 virus was not detected during the examination of newborns, and blood and sputum cultures revealed no growth of pathogenic flora. Subsequently, with standard therapy, the symptoms were quickly relieved, laboratory inflammatory markers returned to normal, and the children were discharged in satisfactory condition.

DISCUSSION

This study highlights the role of NCI in the development of gestational complications and the formation of metabolic disorders. The combination of NCI and GDM in pregnant women is associated with an increased risk of polyhydramnios. GDM was twice as frequent in moderate NCI compared to mild NCI.

The significant correlation between moderate NCI and the presence of GDM during pregnancy, as identified in this study, has a logical explanation. It is well established that normal pregnancy is characterised by a balance between insulin resistance, driven by counterregulatory hormones, and increased insulin production due to hyperactivity of pancreatic β -cells [5]. The SARS-CoV-2 coronavirus binds to angiotensin-converting enzyme type 2 receptors in critical metabolic organs and tissues, including the pancreas and adipose tissue. This interaction results in the development of insulin resistance [6]. A reduction in insulin synthesis and impaired signal transmission

are attributed to the secretion of inflammatory cytokines and the activation of pro-inflammatory signaling pathways, such as TNF- α , IL-6, IL-1 β , C-reactive protein, and NF- κ B [6, 7]. Consequently, the mechanism underlying GDM development following NCI involves direct effect of the virus on cells, insulin resistance development, and systemic inflammation.

According to existing literature, GDM preceding the onset of NCI undoubtedly influences its progression and outcomes. Firstly, hyperglycaemia makes patients with GDM more susceptible to infections, including NCI, by causing immune dysfunction that adversely affects neutrophil chemotaxis, macrophage function, and phagocytic response [8, 9]. Secondly, systemic inflammation during NCI in addition to carbohydrate metabolism disorders can induce metabolic dysregulation and exacerbate the course of viral infections. Furthermore, NCI is more severe in patients who develop GDM concurrently with or prior to SARS-CoV-2 infection compared to those who develop GDM later [10]. Several studies corroborate that gestational DM is a hypercoagulable state [11]. Hyperglycaemia in GDM leads to endothelial dysfunction and platelet activation; when compounded by NCI, this creates a vicious cycle that exacerbates endothelial damage in addition to infection while further aggravating it [12]. This information is supported by evidence linking the development of polyhydramnios in NCI and GDM to the presence of a mutation in the fibrinogen gene.

Polyhydramnios often accompanies the pathological course of pregnancy [13]. The increase in the incidence of polyhydramnios recorded in the study group may have a mixed mechanism. In cases of maternal hyperglycaemia, the increase in fetal urine excretion is, on the one hand, associated with an increase in osmotic diuresis, which contributes to an increase in amniotic fluid production [14]. On the other hand, the increased proinflammatory response characteristic of GDM leads to the acceleration of “physiological ageing” and the terminal form of epithelial-mesenchymal transition in the amniotic membrane, resulting in destabilisation of the matrix and membrane condition, increased production and impaired fluid absorption [15].

The inflammatory response serves as the link between the pathogenesis of viral infection and metabolic disorders. It is logical to assume that any factors modulating inflammation will influence the course of the pathological process. The association of fibrinogen gene polymorphism

with increased amniotic fluid production found in this study aligns with this concept. According to epidemiological and biochemical studies, the *FGB* 455 G-A polymorphism is one of the strongest genetic variations associated with increased plasma fibrinogen [16]. The role of fibrinogen as a modulator not only of coagulation but also of inflammatory processes has been experimentally proven. In addition to local activation of inflammatory reactions at sites of fibrin deposition, a dependence of chronic inflammation in patients with obesity on fibrinogen concentration and the degree of fibrin polymerisation has been documented [4]. Many researchers [17] have also reported the significant role of fibrinogen as a mediator of inflammation in SARS-CoV-2 infection and its close relationship with key proinflammatory cytokines, particularly IL-6. In pregnancy, the proinflammatory contributions of NCI and GDM may be enhanced by fibrinogen hyperproduction due to gene polymorphism present in the patient. “Cytokine storm” products, binding to ACE2 receptors in syncytiotrophoblasts, cytotrophoblasts, and villous endothelium, affect the placenta. The resulting parenchymatous placentitis, intervillous thrombangiitis, perivillitis, and villitis with inflammatory infiltration lead to decreased resorption and increased production of amniotic fluid.

Pathological changes in the mother and the placenta results in alterations to the intrauterine environment. It is known that NCI frequently causes the development of infectious and inflammatory conditions in the fetus. Respiratory disorders, congenital pneumonia, infections during the perinatal period, intraventricular hemorrhage, and hyperbilirubinemia occur significantly more often. The association with NCI demonstrates a clear correlation with the time interval between the infection and the onset of labour [18]. Maternal GDM can lead to the development of diabetic fetopathy, characterised by liver and myocardial dysfunction, as well as a high risk of ante- and intrapartum death if left untreated.

The correlation between the incidence of intrauterine infection (IUI) and associated birth asphyxia in cases where gestational diabetes coexists with maternal NCI during pregnancy aligns more closely with a model of chronic inflammation rather than infectious disease. In accordance with the study design, mothers during the early post-COVID period were excluded from participation. The mean time interval between disease and delivery was 130 days.

The possibility of vertical transmission of the SARS-CoV-2 virus from mother to fetus remains a subject of debate; however, documented cases of viral detection in newborns are rare.

In this study, no instances of NCI births were recorded. An increase in the incidence of intrauterine infection caused by non-specific pathogens in patients with both GDM and NCI is likely. This phenomenon is attributed to the dual negative effects of SARS-CoV-2 virus and hyperglycaemia, manifesting as immune and endothelial dysfunction. These effects lead to increased expression of pro-inflammatory cytokines, heightened vascular permeability, and induction of syncytiotrophoblast apoptosis, resulting in ischaemic damage to the placenta and facilitating the penetration of non-specific pathogens to the fetus [19].

In cases where maternal infectious disease coincides with gestational diabetes, respiratory disorders may arise through several additional pathogenesis pathways, including disruption of surfactant structure, blockade of epithelial sodium channels, and inhibition of nitric oxide synthesis. Clinically, these changes may present as transient tachypnoea or manifest as pneumonia or respiratory distress syndrome.

Studies on respiratory abnormalities in uninfected newborns born to mothers who had contracted coronavirus infection let Man et. al. to describe an immunological pathway for lung damage in the absence of a pathogen. The authors demonstrated that prenatal exposure to SARS-CoV-2 can activate an inflammatory cascade in the newborn's airways, leading to dysregulation of ciliary rhythm in airway epithelium. Proteins such as IL-18, IL-1B, and CASP1 were found to be associated with NLRP3 inflammasome activation in preterm infants with respiratory distress syndrome. Biological processes related to inflammation, chemotactic reactions, and cellular responses—including IL8 production—were significantly elevated in preterm infants. These findings suggest that such changes may underlie the development of fibrosis and allergic diseases during later stages of childhood development [20].

CONCLUSION

The negative impact of factors such as NCI, carbohydrate metabolism disorders, and the development of pre-eclampsia on the course of pregnancy and the condition of the newborn, when considered in isolation, has been well established. This study confirmed that pregnancies and labours in women with NCI, compared to uninfected women,

were more frequently complicated by GDM, pre-eclampsia, preterm labour, and premature detachment of normally situated placenta. The leading role of the systemic inflammatory response, characterised by hyperproduction of pro-inflammatory and anti-angiogenic molecules, is recognised as a universal mechanism underlying all these complications.

Intrauterine fetal hypoxia, which occurs more often in pregnancies complicated by NCI, has been found to increase the risk of antenatal fetal death. Clinically, newborns typically present under the “mask” of an unspecified intrauterine infection, which obscures the vertical transmission of the maternal systemic inflammatory response. The factors determining the likelihood of complications for both mother and fetus are not limited to the characteristics of the pathogen itself — such as the virus strain, its aggressiveness towards cell receptors, and cytokine production — but also include maternal comorbidities, particularly changes in immune and hemostasis systems. This is evidenced by the correlation between the severity of NCI and the probability of developing gestational diabetes, as well as by descriptions of one trigger for polyhydramnios: fibrinogen gene polymorphism, which increases the risk of this complication.

Practical applications of these study findings lie in providing earlier diagnosis of GDM in pregnancies complicated by NCI (and other infectious diseases with similar pathogenesis). Early initiation of specific insulin therapy can help prevent negative outcomes. The timeliness of preventing complications from infectious diseases in pregnant women with underlying metabolic disorders depends on the precision and speed with which pathological and compensatory reactions are assessed. These issues necessitate further detailed investigation. It is likely that omics technologies will hold particular scientific and practical value in advancing this area of research.

REFERENCES

1. Hamming I., Timens W., Bulthuis ML., Lely A.T., Navis G., van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. *Pathology*. 2004;203(2):631–637. DOI: 10.1002/path.1570.
2. Harner D., Gilbert M., Borman R., Clark K.L. Quantitative mRNA expression profiling of ACE 2, a novel homologue of angiotensin converting enzyme. *FEBS Lett*. 2002;4:532(1–2):107–110. DOI: 10.1016/s0014-5793(02)03640-2.
3. Yang J.K., Lin S.S., Ji X.J., Guo L.M. Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes. *Acta Diabetology*. 2010;47(3):193. DOI: 10.1007/s00592-009-0109-4.

4. Luyendyk J.P., Schoenecker J.G., Flick M.J. The multifaceted role of fibrinogen in tissue injury and inflammation. *Blood*. 2019;133(6):511–520. DOI: 10.1182/blood-2018-07-818211.
5. Zhorova V.E., Manasova Z. Sh. Gestational diabetes mellitus: pathogenesis, features of diagnosis and treatment. *Zdorov'e I obrazovanie v XXI veke (Health and Education in the 21st Century)*. 2015;4:367–373. (In Russ.)
6. Suwanwongse K., Shabarek N. Newly diagnosed diabetes mellitus, DKA, and COVID-19: Causality or coincidence? A report of three cases. *Med. Virol.* 2021;93(2):1150–1153. DOI: 10.1002/jmv.26339.
7. Wang Y., Zhang X., Zheng X., Song G., Fang L., Wang Y. et al. Human cytomegalovirus infection and its association with gestational diabetes mellitus during pregnancy. *Peer J*. 2022;15:10:e12934. DOI: 10.7717/peerj.12934.
8. McElwain C.J., McCarthy F.P., McCarthy C.M. Gestational diabetes mellitus and maternal immune dysregulation. *Int. J. Mol. Sci.* 2021;22(8):4261. DOI: 10.3390/ijms22084261.
9. Kleinwechter H.J., Weber K.S., Mingers N., Ramsauer B. Schaefer-Graf U.M., Groten T. et al; COVID-19-Related Obstetric and Neonatal Outcome Study Network. Gestational diabetes mellitus and COVID-19: results from the COVID-19-Related Obstetric and Neonatal Outcome Study. *Am. J. Obstet. Gynecol.* 2022;227(4):631.e1–631.e19. DOI: 10.1016/j.ajog.2022.05.027.
10. Kleinwechter H.J., Weber K.S., Liedtke T.P., Schäfer-Graf U., Groten T., Rüdiger M. et al. COVID-19, pregnancy, and diabetes mellitus. *Z. Geburtshilfe Neonatol.* 2024;228(1):17–31. DOI: 10.1055/a-2180-7715.
11. Teliga-Czajkowska J., Sienko J., Zareba-Szczudlik J., Malinowska-Polubiec A., Romejko-Wolniewicz E., Czajkowski K. Influence of glycemic control on coagulation and lipid metabolism in pregnancies complicated by pregestational and gestational diabetes mellitus. *Adv. Exp. Med. Biol.* 2019;1176:81–88. DOI: 10.1007/5584_2019_382.
12. Bernea E.G., Suica V.I., Uyy E., Cerveanu-Hogas A., Boteanu R.M., Ivan L. et al. Exosome proteomics reveals the deregulation of coagulation, complement and lipid metabolism proteins in gestational diabetes mellitus. *Molecules*. 2022;27(17):5502. DOI: 10.3390/molecules27175502.
13. Boetticher O.A., Zazerskaya I.E., Popova P.V., Vasilyeva E.Yu., Bart V.A. Characteristics of pre-eclampsia in pregnant women with gestational diabetes mellitus. *Zhurnal akusherstva i zhenskikh boleznej (Journal of Obstetrics and Women's Diseases)*. 2019;5:19–36. DOI: 10.17816/JOWD68519-36. (In Russ.)
14. Pagan M., Strebeck R., Dajani N., Sandlin A., Ounpraseuth S., Manning N. et al. Title: is mild idiopathic polyhydramnios associated with an increased risk for an intrauterine fetal demise? *Int. J. Womens Health*. 2023;15:125–134. DOI: 10.2147/IJWH.S386567.
15. Menon R., Behnia F., Poletini J., Richardson L.S. Novel pathways of inflammation in human fetal membranes associated with preterm birth and preterm pre-labor rupture of the membranes. *Semin. Immunopathol.* 2020;42(4):431–450. DOI: 10.1007/s00281-020-00808-x.
16. Hu X., Wang J., Li Y., Wu J., Qiao S., Xu S. et al. The β -fibrinogen gene 455G/A polymorphism associated with cardioembolic stroke in atrial fibrillation with low CHA2DS2-VaSc score. *Sci. Rep.* 2017;7(1):17517. DOI: 10.1038/s41598-017-17537-1.
17. Murugan C., Ramamoorthy S., Kuppuswamy G., Murugan R.K., Sivalingam Y., Sundaramurthy A. COVID-19: A review of newly formed viral clades, pathophysiology, therapeutic strategies and current vaccination tasks. *Int. J. Biol. Macromol.* 2021;193(Pt B):1165–1200. DOI: 10.1016/j.ijbiomac.2021.10.144.
18. Bychkova S.V., Malgina G.B., Dyakova M.M., Chistyakova G.N., Abakarova D.A.. Newborns from mothers who have had COVID-19 during pregnancy: describing critical conditions during the neonatal period. *Pediatrriya im. G.N. Speranskogo (Pediatría n.a. G.N. Speranskogo)*. 2024;103(1):58–65. [DOI:10.24110/0031-403X-2024-103-1-58-65. (In Russ.)]
19. Agostinis C., Toffoli M., Spazzapan M., Balduit A., Zito G., Mangogna A. et al. SARS-CoV-2 modulates virus receptor expression in placenta and can induce trophoblast fusion, inflammation and endothelial permeability. *Front. Immunol.* 2022;13:957224. DOI: 10.3389/fimmu.2022.957224.
20. Man O.M., Azamor T., Cambou M.C., Fuller T.L., Kerin T., Paiola S.G. et al. Respiratory distress in SARS-CoV-2 exposed uninfected neonates followed in the COVID Outcomes in Mother-Infant Pairs (COMP) Study. *Nat. Commun* 15. 2024;399. DOI: 10.1038/s41467-023-44549-5.

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E.M. Matusevich: development of the study concept and design, literature analysis, collection and interpretation of clinical data, database compilation, statistical data processing, drafting the article text, final approval of the manuscript for publication. S.Yu. Yuriev: development of the study concept and design, coordination of the study, drafting the article text, final approval of the manuscript for publication. V.E. Frankevich: development of the study concept and design. N.A. Frankevich: literature analysis, data interpretation, drafting the article text. I.S. Popova: laboratory research. A.A. Kutsenko: collection of clinical material, literature analysis, drafting the article text. A.G. Vasilieva: collection of clinical material, literature analysis, drafting the article text. D.R. Melikh: collection of clinical material. N.D. Zimina: database compilation, statistical data processing.

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