ANALYSIS OF THE RISK FACTORS OF PERINATAL PATHOLOGY IN WOMEN WHO HAD COVID-19 DURING PREGNANCY

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Summary

The aim of this study is to look at the impact of COVID-19 on the occurrence of perinatal complications in women who contracted COVID-19 during pregnancy, among the population of the Lviv region. Data on the results of medical and social characteristics, somatic and reproductive anamnesis, and the course of pregnancy of women who contracted COVID-19 during pregnancy (the main group) were analyzed. 20.0% of women who contracted COVID-19 during pregnancy were aged 36 years or older, while there were no women of this age in the control group ($p< 0.05$). The majority of pregnant women who contracted COVID-19 during pregnancy, namely 68.0% lived in the city, and the majority of healthy pregnant women in the control group lived in rural areas, namely 70.0% ($p <0.05$). According to social status, a significant part of the women of the main group, namely 30.0% were employed, compared to the women of the control group, where only 16.7% or ($p<0.05$) were employed.

24.0% of women in the main group had certain peculiarities in their reproductive anamnesis and 52.0% of them had somatic diseases. None of the women in the control group had reproductive or somatic history of complications. All women in the main group had a complicated course of pregnancy, in particular, 30.0% of women had preeclampsia, 28.0% had anemia of various degrees, 52.0% of pregnant women had combined complications, and 16.0% of women had an exacerbation of somatic pathology. In the control group, 90.0% of women did not have a complicated course of pregnancy. The majority of pregnant women (96.0%) fell ill with COVID-19 in the 3rd trimester of pregnancy, and only 4.0% of people – in the 2nd trimester. About half of the women (54.0%) had a mild course of COVID-19, 38.0% of pregnant women had a moderate course of the disease, and 8.0% had a severe course of the disease. Therefore, women over 36 years, living in an urbanized area with somatic pathology and complicated course of pregnancy can be considered as risk factors for perinatal complications for pregnant women with COVID-19.

Key words: pregnancy, pregnant women, COVID-19.

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1. Introduction

In recent years, all over the world, close attention has been paid to improving the health of new generations *(Zhylka N.Ya. et al., 2021)*. The quality of providing medical care to the fetus and newborn in the perinatal period is one of the integral indicators of the quality of all medical care in the country. The perinatal period is unique in its importance for the development of the health of the child and, therefore cannot be compared with any other period of life *(Veropotvelyan P. N., 2017)*.

From the point of view of finding reserves for improving the quality of care in the perinatal period and assessing the structure of perinatal mortality, the so-called perinatal audit should be considered. It allows to identify cases of perinatal mortality that could potentially be avoided *(Kovalenko O. S., 2016)*.

According to the world literature, perinatal complications in the population occur in 30-45% of cases, and among pregnant women with a complicated obstetric and gynecological history, they reach 75%. Complications are more frequent when pregnancy is combined with extragenital pathology, namely in 25-45% of cases, and in pregnant women who have suffered a viral or bacterial infection, namely in more than 60% of cases *(Schwartz D. A., 2020)*.

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome due to infection with the SARS-CoV-2 coronavirus, has spread rapidly around the world and on March 12, 2020, the WHO declared the outbreak a pandemic *(Guan W. J. et al., 2020)*. Since pregnant women have a higher risk of a complicated course of coronavirus infection, they have been identified as a vulnerable group *(Shkolnyk O.S. et al., 2021; Wang P. H. et al., 2021)*.

Data from the literature shows that pregnant women with COVID -19 have a higher risk of miscarriage, premature birth, preeclampsia, and operative delivery, especially in cases where the disease was complicated by pneumonia *(Wang P. H. et al., 2021)*. Pregnant women are in a state of physiological immunodepression, therefore, they may have an increased risk of developing a severe course of the disease of COVID -19, in particular, pneumonia and respiratory failure *(Wang P.H. et al., 2021)*.

At the moment, there is a very limited amount of information about the risks associated with coronavirus infection in the first and second trimesters. There is mixed data regarding the risk of congenital malformations in newborns born to mothers with fever. However, there is insufficient literature on the impact of COVID -19 on the risk of pregnancy complications. So far the data on this epidemic is reassuring in the sense that there is no increased risk of fetal loss or congenital anomalies associated with infection in early pregnancy *(Hui D. S. et al., 2020; Bai Y. et al., 2020)*. No evidence of the virus was found COVID -19 in amniotic fluid or umbilical cord blood of infants born to infected women *(Jaiswal N. et al., 2021)*. For those who become ill later in pregnancy, sonographic assessment of fetal growth in the third trimester should also be considered *(Kannan S. et al., 2020)*.

At the moment we are all witnesses and participants of the COVID-19 pandemic, which is in the stage of development. The majority of doctors have not dealt with coronavirus infection before, which forces them to develop new tactics of preventive and curative measures.

According to the recommendation of the National Health Commission of China, it is necessary to monitor pregnant women, including after recovery, and to isolate the child from the sick mother for 14 days after birth (*Holubovs'ka O. A., 2021; Chen D. et al., 2020*). In most people, the disease has a mild or moderate course. About 15% of cases of the disease have a severe course with the need to use oxygen therapy and in 5% – the condition of patients is critical. The mortality rate due to infection with COVID-19 is on average 4.5 % and there are reports of an extremely low mortality rate (for example, 0.37% in Germany). A more severe or fatal course is more often observed in older people and with concomitant diseases, which requires intensive therapy and prolonged rehabilitation *(Bai Y. et al., 2020; Holubovs'ka O. A., 2021; Chen D. et al., 2020)*.

Despite a large and rapidly growing number of cases of COVID -19 and deaths caused by it, data on clinical characteristics of pregnant women wis limited. Viral pneumonia is one of leading causes of death of pregnant women in all over the world *(Panahi L. et al., 2020)*.

Physiological changes that occur during pregnancy make a woman more vulnerable to severe infections. In general, pregnancy is a state characterized by weakened immunity, in which cardiovascular needs are increased. The state of compensated respiratory alkalosis combined with metabolic acidosis makes women vulnerable to respiratory diseases such as COVID-19 *(Juusela A. et al., 2020)*. Anatomical changes, such as an increase in the transverse diameter of the chest and an increased level of the diaphragm, reduce the resistance of a pregnant woman to hypoxia. Changes in lung volume and vasodilatation can lead to swelling of the mucous membrane and increased secretion in the upper respiratory tract. In addition, changes in cellular immunity increase the susceptibility of pregnant women to infection with intracellular organisms such as viruses. As for the fetus and the newborn, the immaturity of the innate adaptive function of the immune system makes them very vulnerable to infections *(Delahoy M. J. et al., 2020)*.

In severe cases of COVID-19, a cytokine storm is thought to be associated with systemic tissue destruction and subsequent poor prognosis. However, to date there are no reports of pregnant women predisposed to cytokine release syndrome caused by COVID-19 *(Hayakawa S. et al., 2020)*. Severe acute respiratory distress syndrome during SARS-CoV-2 infection during pregnancy is not associated with an increased risk of spontaneous abortion and spontaneous premature birth. However, fever and hypoxemia may increase the risk of preterm birth, premature rupture of membranes, and abnormal fetal heart rhythms. But premature birth can occur in patients with COVID-19 without severe respiratory diseases *(Elshafeey F. et al., 2020)*.

In this regard, the development of an algorithm of rehabilitation treatment and preventive measures for such women who suffered from COVID-19 during pregnancy is of great importance for perinatal complications *(Berghella V. et al., 2020; Kostiuk O.O. et al., 2020)*.

Taking into account the above, it was decided that it was appropriate to conduct a study of risk factors for perinatal complications in women who contracted COVID-19 during pregnancy and to determine the impact of this disease on the structure of the main obstetric indicators in the population of the Lviv region of Ukraine.

The objective of the study is to look at the impact of COVID-19 on the occurrence of perinatal complications in women who contracted this disease during pregnancy, among the population of Lviv region. To solve this goal, the following tasks were set:

1. To study the medical and social characteristics of women who contracted COVID-19 during pregnancy.
2. To investigate the peculiarities of the somatic and reproductive anamnesis of women who contracted COVID-19 during pregnancy.
3. To conduct an analysis of risk factors for perinatal complications in women with pathology who contracted COVID-19 during pregnancy.

2. The results

Medical records of 50 women aged 16–45 years (average age was 27.1±3.7) who contracted COVID-19 during pregnancy (main group) were selected. Comparisons were made with similar parameters of women in the control group. The control group included 30 pregnant women, aged 16–43 years (average age was 26.3±3.8), who turned to medical institutions in the city of Lviv and the Lviv region in the same period of time, and did not suffer from COVID-19 during pregnancy and had no complications of reproductive and somatic history (year 2021). In the course of the study, age parameters, social status, somatic and reproductive anamnesis data, course of pregnancy were studied. Statistical processing of the obtained results was carried

out using the package of application programs "Statistica 7.0", namely standard package of statistical analysis Excel 2013. Credibility between different groups was investigated according to the Pearson χ^2 test. Differences were considered probable at a significance level of $p<0.05$.

Distribution by age and social status of women

The study of the primary medical documentation showed that the age of the examined women ranged from 16 to 36 years and old. The age characteristics and social status of women of both groups are presented in Table 1.

Table 1

Age characteristics and social status of women of both groups

Indexes	Groups of patients		Statistical indicators
	The main one n=50	Control n=30	
Age characteristics of women (years, n/%)			
16-20	-	3 (10.0)	χ^2=5.195; P=0.04942; P < 0.05
21-25	7 (14.0)	10 (33.3)	χ^2=4.188; P=0.0514; P>0.05
26-30	17 (34.0)	12 (40.0)	χ^2= 0.29 ; P=0.63595; P>0.05
31-35	16 (32.0)	5 (16.7)	χ^2=2.277; P=0.18998; P>0.05
36 and over	10 (20.0)	-	χ^2=6.857; P=0.01105; P < 0.05
Social status of women			
Residents of the city	34 (68.0)	9 (30.0)	χ^2=10.891; P=0.00114; r< 0.05 _
Rural settlers	16 (32.0)	21 (70.0)	χ^2=10.891; P=0.00124; p < 0.05
White colar women	15 (30.0)	5 (16.7)	χ^2=1.778; P=0.28599; p>0.05
Housewives	26 (52.0)	15 (50.0)	χ^2=0.030; P=1.00000; p > 0.05
Blue colar workers	9 (18.0)	10 (33.3)	χ^2=2.434; P=0.17429; p>0.05

Note: p is the statistical significance of the differences in the indicators of the main group compared to the control group

Established reliable differences were found in the age groups of 16–20 years: there were no such persons in the main group, and 3 (10.0%) in the control group, as well as in the group aged 36 years and older – 10 (20.0%) in the main group and no of such persons in the control group, respectively ($p< 0.05$, Table 1). In other age groups, no significant difference between the indicators of women in both groups was found ($p>0.05$).

The study of the place of residence and social status of women of both groups showed that the majority of pregnant women who contracted COVID-19 lived in the city 34 (68.0%), and the majority of healthy pregnant women of the control group lived in rural areas 21 (70.0%) ($p <0.05$, Table 1). In both groups, the majority of pregnant women were housewives – 26 (52.0%) in the main group versus 15 (50.0%) in the control group. No significant changes were found in other social indicators: the smallest number of women in the main group worked blue collar workers- 9 (18%) versus 10 (33.3%) in the control group ($p > 0.05$). There were also more white collar workers in the main group – 15 (30%) against 5 (16.7%) in the control group, although without significant difference ($p > 0.05$, Table 1).

Peculiarities of the reproductive and somatic anamnesis of women who contracted COVID-19 during pregnancy

The analysis of reproductive history data showed that in 38 (76.0%) women the reproductive and somatic anamnesis was not uncomplicated, and 12 (24.0%) women of the main

group had certain peculiarities in reproductive function. Thus, spontaneous miscarriages or frozen pregnancies were noted in 9 (18.0%) people, stillbirth in 2 (4.0%) women, infertility in the anamnesis in 1 (2.0%) woman. In the control group, all women had no history of reproductive complications.

About half of the women in the main group had somatic pathology. Thus, 24 (48.0%) women of the main group had no complications of somatic anamnesis, and 26 (52.0%) patients had somatic diseases.

It was proved that in the structure of somatic pathology, pregnant women of the main group had a history of other diseases either separately or in parallel with COVID-19. Pneumonia of various localization was the most common and was diagnosed in 9 (18.0%) of women; pathology of the urinary system (chronic kidney diseases and acute pyelonephritis during pregnancy) was diagnosed in 8 (16.0%) pregnant women, and thyroid disease (diffuse goiters and hormonal disorders in the form of autoimmune and hypo – and hyperthyroidism) was diagnosed in 5 (10.0%) pregnant women. In the list of somatic diseases of these women, 2 (4.0%) cases of pathology of the cardiovascular system and diabetes were noted. The pregnant women of the control group had no somatic pathology.

The course of pregnancy in women who contracted COVID-19 during pregnancy

A detailed analysis of the course of pregnancy in women of both groups showed that all pregnant women of the main group had a complicated course of pregnancy, in particular, in 15 (30.0%) women, the pregnancy was complicated by preeclampsia, in 14 (28.0%) by anemia of various degrees, 26 (52.0 %) women had combined complications, and in 8 (16.0%) pregnant women, exacerbation of somatic pathology was noted. In the control group, 27 (90.0%) women had an uncomplicated pregnancy, and isolated complications were noted in only 3 (10.0%) cases: one (3.3%) woman had early preeclampsia and two (6.7%) developed mild pregnancy anemia ($p < 0.05$, table 2).

Table 2

The course of pregnancy in women of the examined groups

Indexes	Main group 50 (n /%)	Control group 30 (n /%)	Statistical indicators
Uncomplicated course of pregnancy	-	27(90.0)	χ^2=67.925; R <0.001 ; p<0.05
Complicated course of pregnancy	50(100.0)	-	χ^2=80,000; P<0.001; p<0.05
Early gestosis	3(6.0)	1 (3.3)	χ^2=0.281; P=1.00000; p > 0.05
The threat of premature birth	4(8.0)	-	χ^2=2.526; P=0.29129; p > 0.05
Anemia of pregnant women	14 (28.0)	2 (6.7)	χ^2=5.333; P=0.02295; p<0.05
Preeclampsia	15(30.0)	-	χ^2=11.077; P=0.00062; p<0.05
Respiratory viral infection	4(8.0)	-	χ^2=2.526; P=0.29129; p > 0.05
Exacerbation of somatic pathology	8(16.0)	-	χ^2=5.333; P=0.02223; p<0.05
Combined complications	26(52.0)	-	χ^2=23.111; R <0.001 ; p<0.05
Complicated somatic history	26(52.0)	-	χ^2=23.111; R <0.001 ; p<0.05
Uncomplicated somatic history	24(48.0)	-	χ^2=23.111; R <0.001 ; p<0.05

Note: p is the statistical significance of the differences in the indicators of the main group compared to the control group

Analysis of data on the period of gestation, when a pregnant woman received a positive test for COVID-19 and confirmed the diagnosis showed that the largest number of people fell ill in the 3rd trimester of pregnancy, 48 (96.0%) women and only 2 (4.0%) fell ill in the 2nd trimester while there were no women who fell ill in the 1st trimester in our group. In the majority of pregnant women, namely in 27 (54.0%) women COVID-19 was in a mild form, in 19 (38.0%) of pregnant women the course of the disease was of moderate severity, and in 4 (8.0%) the course of the disease was in a severe form (Table 3).

Table 3

Gestation period during COVID-19

Indexes	Main group (n/%)	
	n	%
Gestation term		
And the trimester	-	-
II trimester	2	4.0
III trimester	48	96.0
The course of COVID-19		
The course of COVID-19 is mild	27	54.0
Medium difficulty	19	38.0
Difficult	4	8.0
The main biochemical indicators of COVID-19		
D – dimer Less 0.04	21	42.0
D – dimer above 0.04	29	58.0
Procalcitonin less than 0.01	22	44.0
Procalcitonin above 0.01	28	56.0

The study of the data of the main biochemical indicators, which determined the generally accepted treatment tactics and the severity of the course of the disease, showed that almost the same number of women had reduced procalcitonin and D – dimer levels, namely 21 (42.0%) and 22 (44.0%), and the same number of women had elevated levels of procalcitonin, namely 28 (56.0%) and D-dimer level, namely 29 (58.0%), which was the main factor in determining the severity of the course of COVID-19. 27 (54.0%) pregnant women had a mild course of the disease, and 23 (46.0%) – heavy and medium course of the disease.

3. Conclusions

1. Significant differences were established in the age groups of 16–20 years old. There were no persons of this age in the main group, while there were only 3 (10.0%) in the control group. 10 (20.0%) of women were from 36 years old in the main group in the control group there were no women above 36 years old ($p<0.05$). In other age groups, no significant difference between the indicators of women in both groups was found ($p>0.05$).

2. The majority of pregnant women who contracted HIV – 19 during pregnancy lived in the city – 34 (68.0%), and the majority of healthy pregnant women of the control group lived in rural areas 21 (70.0%), ($p<0.05$). By social status, a significant part of women in the main group were employed compared to women in the control group: 15 (30.0%) versus 5 (16.7%).

3. In 12 (24.0%) women of the main group certain peculiarities of the reproductive history were established: spontaneous miscarriages or frozen pregnancies were noted in 9 (18.0%)

people, stillbirth in 2 (4.0%), infertility in 1 (2.0%) woman. All women of the control group had no reproductive history of complications.

4. 26 (52.0%) women of the main group had somatic diseases. In the structure of somatic pathology, pneumonia of various localization was the most common, namely 9 (18.0%) women were ill with it; 8 (16.0%) of pregnant women had pathology of the urinary system (chronic kidney diseases and acute pyelonephritis during pregnancy); 5 (10.0%) women had diseases of the thyroid gland (diffuse goiters and hormonal disorders in the form of autoimmune and hypo- and hyperthyroidism); and 2 (4.0%) women had cases of pathology of the cardiovascular system and diabetes. The pregnant women of the control group had no somatic pathology.

5. All women of the main group had a complicated course of pregnancy, in particular, 15 (30%) women had preeclampsia, 14 (28.0%) had anemia of various degrees, 26 (52.0%) pregnant women had combined complications, and 8 (16.0%) persons had an exacerbation of somatic pathology. In the control group, 27 (90.0%) had an uncomplicated pregnancy, one woman noted early preeclampsi, and two developed mild pregnancy anemia.

6. Most pregnant women fell ill with COVID-19 in the 3rd trimester of pregnancy, 48 (96.0%) women and only 2 (4.0%) fell ill in the 2nd trimester while there were no women who fell ill in the 1st trimester in our group. About half of the women, 27 (54.0%) had a mild course of COVID-19 and in 19 (38.0%) pregnant women the course of disease was of moderate severity and in 4 (8.0%) the course of the disease was in a severe form.

7. Age characteristics (over 36 years old), social status (living in an urbanized area), the presence of somatic pathology, which leads to a significant number of complications during pregnancy, can probably be considered risk factors for perinatal complications in pregnant women with COVID-19.

Prospects for further research

For further research, it is planned to expand the list of women who were will with COVID-19 during pregnancy in order to study the informative spectrum of risk factors for perinatal complications (results of termination of pregnancy, the course of childbirth and the condition of the newborn). Such study would determine the impact of COVID-19 on the reproductive potential of Lviv region population.

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