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ASSESSMENT OF REPRODUCTIVE FUNCTION OF WOMEN WHO HAVE SURVIVED COVID-19

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S U M M A R Y

Introduction. Coronavirus disease (Covid-19) which has been planetary in nature since 2019 has had a negative impact on public health. The impact of Covid-19 on women's reproductive health is also a hot topic among researchers in the last 5 years post Covid-19, as there are mixed opinions of researchers on the impact of coronavirus infection on women's reproductive organs.

Objective of the study. To assess the impact degree of coronavirus infection on the reproductive function of women.

Material and methods. The study included 180 women of reproductive age, the main group consisted of 90 women with moderate to severe coronavirus infection, confirmed case of Covid-19: positive PCR RNA SARSCoV-2, lower respiratory tract lesions (Covid-associated pneumonia) according to CT 1-4. The control group consisted of 90 women who were not infected with coronavirus infection.

Results. The mean age of the patients was 31±9 years. The analysis showed that women who had undergone coronavirus infection had reproductive disorders such as menstrual disorders, difficulties with pregnancy conception, and high rates of spontaneous miscarriages after coronavirus infection.

Discussion. This study shows that moderate to severe coronavirus infection can affect reproductive health. Menstrual irregularities observed in 68.8% of patients may be due to the effects of the virus on the hypothalamic-pituitary-ovarian system. The obtained results demonstrated the correlation between coronavirus infection and difficulties with conception in the studied groups of patients.

Conclusions. The results of the present study indicate statistically significant effects of Covid-19 on the female reproductive system. Covid-19 infection potentially results in menstrual irregularities, adversely affects pregnancy and increases the risk of spontaneous miscarriage.

Keywords: Covid-19, SARS-CoV-2, coronavirus infection, female reproductive function, pregnancy, labor.

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Т Ұ Ж Ы Р Ы М

COVID-19-ДАН ӨТКЕН ӘЙЕЛДЕРДІҢ РЕПРОДУКТИВТІ ҚЫЗМЕТІН БАҒАЛАУ

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Кіріспе. 2019 жылдан бері планеталық сипатқа ие болған коронавирус ауруы (Covid-19) халықтың денсаулығына кері әсерін тигізді. Covid-19-ның әйелдердің ұрпақты болу денсаулығына әсері Covid-19 дан кейінгі кезеңнің соңғы 5 жылындағы зерттеушілер арасында да өзекті болды, өйткені зерттеушілер арасында коронавирустық инфекцияның әйелдердің ұрпақты болу органдарына әсері туралы әртүрлі пікірлер бар.

Зерттеудің мақсаты. Әйелдердің ұрпақты болу функциясына коронавирустық инфекцияның әсер ету дәрежесін бағалау.

Зерттеудің материалдары мен әдістері. Зерттеуге репродуктивті жастағы 180 әйел қатысты, негізгі топқа орташа және ауыр коронавирустық инфекциядан айыққан 90 әйел, расталған Covid-19 жағдайы: SARSCoV-2 РНҚ ПТР оң нәтижесі, төменгі тыныс жолдарының зақымдануы. (Covid-19- пен байланысты пневмония) КТ деректеріне сәйкес 1-4. Бақылау тобына коронавирус инфекциясын жұқтырмаған 90 әйел кірді.

Зерттеу нәтижелері. Науқастардың орташа жасы 31±9 жасты құрады. Сараптама көрсеткендей, коронавирустық инфекциямен ауырған әйелдерде етеккір циклінің бұзылуы, жүкті болуды қиындатқар, сондай-ақ коронавирустық инфекциядан кейінгі өздігінен түсіктердің жоғары деңгейі сияқты ұрпақты болу функцияларында бұзылулар болған.

Талқылау. Бұл зерттеу орташа және ауыр коронавирустық инфекция репродуктивті денсаулыққа әсер етуі мүмкін екенін көрсетеді. Етеккір циклінің бұзылуы пациенттердің 68,8% – байқалатындар вирустың гипоталамус-гипофиз-аналық без жүйесіне әсерінен болуы мүмкін. Нәтижелер пациенттердің зерттелетін топтарында коронавирустық инфекцияның тұжырымдамамен күрделілігімен байланысының болуын көрсетті.

Қорытынды. Зерттеу нәтижелері әйелдердің ұрпақты болу жүйесі үшін Covid-19-ның статистикалық маңызды салдарын көрсетеді. Бұрынғы Covid-19 инфекциясы етеккір циклінің бұзылуына әкелуі мүмкін, жүктілік ағымына теріс әсер етеді және өздігінен түсік түсіру қаупін арттырады.

Негізгі сөздер: Covid-19, SARS-CoV-2, коронавирустық инфекция, әйелдердің репродуктивті қызметі, жүктілік, босану.

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РЕЗЮМЕ

ОЦЕНКА РЕПРОДУКТИВНОЙ ФУНКЦИИ ЖЕНЩИН, ПЕРЕНЕСШИХ COVID-19

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Введение. Коронавирусная болезнь (Covid-19), носившая планетарный характер с 2019 года, оказала негативное влияние на здоровье населения. Влияние Covid-19 на репродуктивное здоровье женщин остается актуальным для исследователей в течение последних 5 лет постковидного периода, поскольку существуют разнонаправленные мнения относительно воздействия коронавирусной инфекции на репродуктивные органы женщин.

Цель исследования. Оценка степени влияния коронавирусной инфекции на репродуктивную функцию женщин.

Материал и методы. В исследование включено 180 женщин репродуктивного возраста. Основную группу составили 90 женщин, переболевших коронавирусной инфекцией средней и тяжелой степени. Подтвержденными случаями Covid-19 считались положительные результаты ПЦР на РНК SARS-CoV-2, а также наличие поражения нижних дыхательных путей (Covid-ассоциированные пневмонии) по данным КТ в степени 1-4. Контрольную группу составили 90 женщин, неинфицированных коронавирусной инфекцией.

Результаты исследования. Средний возраст пациентов составил 31±9 лет. Проведенный анализ показал, что женщины, перенесшие коронавирусную инфекцию, испытывали нарушения в репродуктивной функции, такие как нарушение менструального цикла, трудности с зачатием беременности, а также высокие показатели самопроизвольных выкидышей после перенесенной коронавирусной инфекции.

Обсуждение результатов. Исследование показывает, что коронавирусная инфекция, перенесенная в средней и тяжелой степенях тяжести может повлиять на репродуктивное здоровье. Нарушение менструального цикла, наблюдаемое у 68,8% пациенток, может быть вызвано воздействием вируса на гипоталамо-гипофизарно-яичниковую систему. Полученные результаты продемонстрировали наличие взаимосвязи коронавирусной инфекции со сложностями с зачатием у обследуемых групп пациентов.

Выводы. Результаты проведенного исследования указывают на статистически значимые воздействия Covid-19 на репродуктивную систему женщин. Перенесенная инфекция Covid-19 потенциально приводит к нарушению менструального цикла, негативно влияет на течение беременности и повышает риск самопроизвольного выкидыша.

Ключевые слова: Covid-19, SARS-CoV-2, коронавирусная инфекция, репродуктивная функция женщин, беременность, роды.

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INTRODUCTION

Coronavirus disease (Covid-19) which has been planetary in nature since 2019 has had a negative impact on public health. The impact of Covid-19 on women's reproductive health is also a hot topic among researchers in the last 5 years of post Covid-19 period, as there are mixed opinions of researchers on the impact of coronavirus infection on women's reproductive organs.

It was found in studies of the SARS-CoV-2 virus that endothelial tissue suffers damage [1, 2]. Endothelial dysfunction is manifested by an increase in endothelium permeability, increased synthesis of prothrombogenic factors, and activation of immune system cells. All these processes are systemic in nature and affect the entire vasculature. They can explain the multiorgan changes in Covid-19 [3].

It was found in studies by R. Li et al. that the SARS-CoV-2 virus affects the reproductive system of women [4]. The impact of SARS-CoV-2 on ovarian granulosa cells decreases the quality of oocyte. There is every reason to believe that this can lead to miscarriages. In turn, repeated pregnancy

loss results in damage to endometrial endothelial cells, affects embryo implantation and results in infertility [5, 12]. There is an increase in the percentage of losses both in natural cycles and in in vitro fertilization cycles in the early stages of pregnancy. Given the lack of evidence on the direct impact of the virus on ovarian and endometrial tissue, studies on SARS-CoV-2 in this direction are currently ongoing.

The impact of Covid-19 on the reproductive system of women can be mediated by the toxic effects of the drugs used, the duration of hospitalization in the intensive care unit, and decompensation of concomitant chronic diseases [6-10].

It is currently unknown what long-term consequences for women's reproductive health may be associated with Covid-19. In this regard, all women who have had Covid-19, especially in severe form, should be classified as a high-risk group for development of complications and undergo more careful clinical monitoring for 1 year after hospital treatment for Covid-19. It is required to determine further management tactics: restoration of the menstrual cycle, treatment of infertility, surgical treatment of gynecological pathology, selection

of birth control methods, hormone replacement therapy and other specific therapy for gynecological issues.

Objective of the study – to assess the impact degree of coronavirus infection on the reproductive function of women.

MATERIAL AND METHODS

The study included 180 women of reproductive age. The main group consisted of 90 women with moderate to severe coronavirus infection. Positive PCR RNA SARS-CoV-2, as well as lower respiratory tract lesions (Covid-associated pneumonia) according to CT 1-4 were considered as confirmed cases of Covid-19. The control group included 90 women not infected with coronavirus. The age of the patients was from 20 to 40 years, mean age was 31 ± 9 years. The exclusion criterion was women not planning pregnancy.

The primary stage of the study was a retrospective analysis of clinical cases of pregnancies, childbirth and the postpartum period in women who had coronavirus infection in

the period from 2020 to 2021. Information was collected by copying data from medical records from the archives of the Unitary Enterprise based on the Right of Economic Management “Multidisciplinary Regional Hospital No. 2” of the Astana Akimat. The data on women from the control group were taken from the Complex Medical Information System of the Unitary Enterprise based on the Right of Economic Management “Multidisciplinary Regional Hospital No. 2” of the Astana Akimat.

The data was analyzed with the use of descriptive statistics, and percentage analysis was used for comparisons.

RESULTS OF THE STUDY

The mean age of the patients was 31 ± 9 years. Such disorders as amenorrhea, dysmenorrhea, and abnormal uterine bleeding were identified and studied among the menstrual disorders in women of the main group and the control group. Their comparative analysis was performed. Data on the disorders are shown in Table 1.

Table 1 – Menstrual disorders in women

Disorders	Main group		Control group	
	absolute value	relative value	absolute value	relative value
Amenorrhea	41	45.56%	12	13.3%
Dysmenorrhea	28	31.1%	9	10%
Abnormal uterine bleeding	11	12.2%	3	3.3%

Note: compiled by the author based on their own research

Thus, the number of women with such menstrual disorders as amenorrhea in the main group was twice larger than the number in the control group – 26.6 ± 15 ($p \leq 0.05$). There were three times more women with dysmenorrhea in the main group than in the control group. Menstrual disorders plotted against time are shown in Figure 1.

The next indicator that we studied was the ability to conceive after a coronavirus infection. A comparative analysis of the groups was performed depending on the occurrence of pregnancy within 1 year, 2 years and 3 years. Data on pregnancy occurrence are shown in Table 2.

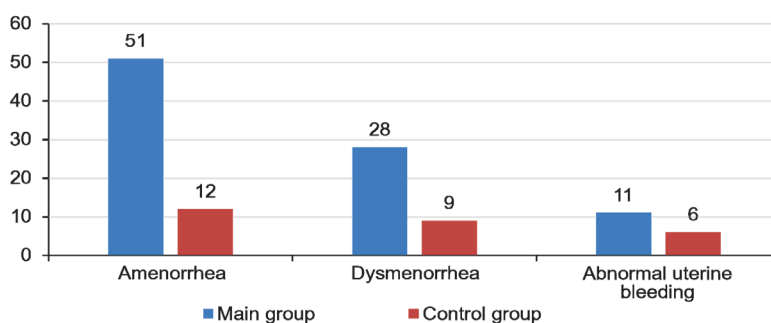


Figure 1 – Menstrual disorders in women with Covid-19

Table 2 – Pregnancy occurrence

Pregnancy	Main group		Control group	
	absolute value	relative value	absolute value	relative value
Within 1 year	26	28.8%	54	60%
Within 2 years	31	34.4%	16	17.7%
Within 3 years	23	25.5%	8	8.9%
Did not occur	9	10%	2	2.2%

Note: compiled by the author based on their own research

Thus, the number of women in the control group who became pregnant within a year during pregnancy planning was 2.5 times higher than in women in the main group – 40 ± 14 ($p \leq 0.05$).

It should be noted that pregnancy occurred within 2 years (41 or 45.5%) and within 3 years (23 or 25.5%) after planning pregnancy among women in the main group. Pregnancy did not occur in 9 women (10%) (Fig. 2).

The analysis of pregnancy outcomes included early and late spontaneous miscarriages, missed miscarriages. Data on pregnancy outcomes are shown in Table 3.

Thus, the number of early spontaneous miscarriages in the main group was 3 times higher than the number of miscarriages in women in the control group – 16 ± 8 ($p \leq 0.05$). Missed miscarriage in the control group was registered in 11 women (Fig. 3).

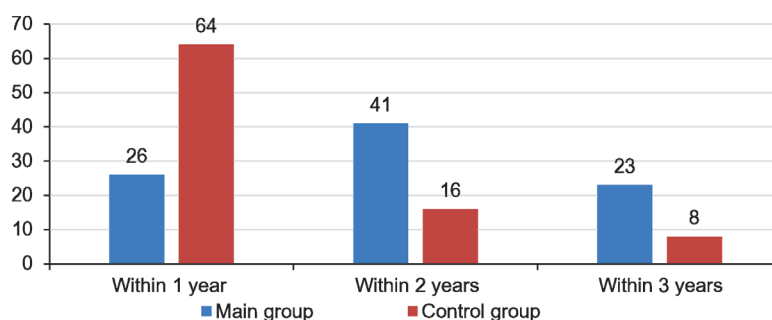


Figure 2 – Pregnancy occurrence period in women who have had Covid-19

Table 3 – Pregnancy outcomes

Spontaneous miscarriage	Main group		Control group	
	Absolute value	Relative value	Absolute value	Relative value
Before week 12	24	26.6%	8	8.8%
Before week 22	8	8.8%	3	3.3%
Missed miscarriage	11	12.2%	2	2.2%

Note: compiled by the author based on their own research

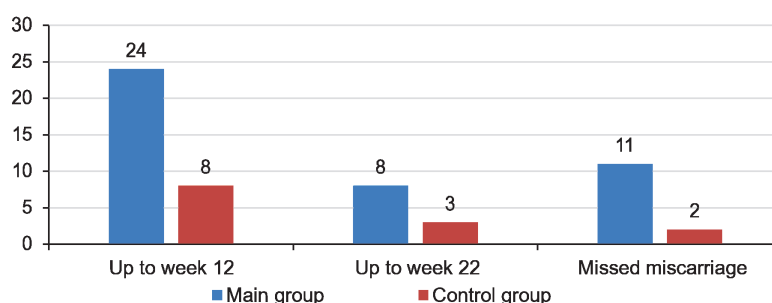


Figure 3 – Pregnancy outcomes

DISCUSSION OF THE RESULTS

This study shows that moderate to severe coronavirus infection can affect reproductive health. Menstrual irregularities observed in 68.8% of patients may be due to the effects of the virus on the hypothalamic-pituitary-ovarian system [12]. Given the high level of ACE2 expression in the endometrium, it is possible that the SARS-CoV-2 virus can penetrate the stromal cells of this layer, which can lead to pathological manifestations in women with COVID-19. In turn, they may be at increased risk of early pregnancy loss [13].

CONCLUSIONS

The analysis demonstrated that women who have had coronavirus infection had the following reproductive dysfunctions:

- menstrual disorder was observed in 62 (68.8%) women ($p \leq 0.05$);
- difficulties with conception: pregnancy occurred within a year after coronavirus infection when planning pregnancy within a year in 26 (28.8%) women ($p \leq 0.05$), within two years – in 41 (45.5%) women ($p \leq 0.05$) and within three years – in 23 (25.5%) women ($p \leq 0.05$), pregnancy did not occur in 9 (10%) women ($p \leq 0.05$);
- early and late spontaneous miscarriages after the illness were registered in 41 (45.5%) women ($p \leq 0.05$).

Thus, the results of the study show statistically significant consequences of Covid-19 for a woman's reproductive system. Covid-19 infection potentially results in menstrual disorders, negatively affects the course of pregnancy and increases the risk of spontaneous miscarriage.

Research transparency

There was no funding from outside organizations or medical representatives during this work.

Declaration of financial and other interests

The final version of the manuscript was approved by all authors. The authors did not receive any royalties for the article. The authors are solely responsible for submitting the final version of the manuscript for publication.

Contribution of the authors

Kozhanazarova Aziza Dzhanbekovna – drafting, data collection and analysis, editing;

Iskakov Serik Sayatovich – conceptualization, methodology, verification, editing.

Conflict of interests

The authors declare no conflict of interest.

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The authors confirm that this scientific article has not been published anywhere before.

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