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# Evaluation of the Treatment of Pregnant Women with COVID-19 Using the Drug Baricitinib

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## Abstract

This article discusses the complexities and various aspects related to the treatment of pregnant women with COVID-19. The experience of Chinese doctors who were the first to face this problem is considered, and a new method of treating the disease using the drug Baricitinib is also considered. Baricitinib is an anti-inflammatory drug, a representative of the Janus kinase class, used in the treatment of rheumatoid arthritis. It blocks intracellular signaling pathways, which leads to the regulation of the synthesis of interleukins 2, 6, 10, and interferon-gamma. The drug is licensed for the treatment of rheumatoid arthritis, has good efficacy and safety indicators. Attention was paid to the doses and modes of use of baricitinib. The article discusses a study conducted by Chinese doctors. The study involved 34 infected pregnant women, of whom half were offered standard treatment and the other half standard treatment with baricitinib. In order to have a complete picture that allows us to conclude that this method of treatment is ineffective or effective, it is necessary to continue monitoring patients who took baracitinib in the treatment of COVID-19.

**Keywords:** *COVID-19, Pregnancy, Baricitinib, Drug*

## Introduction

Humanity suddenly faced the COVID-19 epidemic. In order to reduce the number of victims, the authorities of various countries had to take all sorts of unprecedented measures, including the closure of long-distance and international borders and the introduction of quarantines (Rauf *et al*., 2020). Another problem that doctors had to face was a large number of COVID-19-infected people who had various diseases and complications not directly related to this infection (Ayivi *et al*., 2021).

The treatment of pregnant women infected with COVID-19 required special attention (Magomedov *et al*., 2021; Mishununa *et al*., 2021). It was necessary to find a way to treat pregnant patients without harm to the fetus. For the treatment of pregnant women with COVID-19, various methods and drugs were used, which were selected in such a way as to maximize the benefits and minimize harm to the fetus (Suleimanova *et al*., 2021). One of the drugs that they decided to use for the treatment of pregnant women with COVID-19 was Baricitinib. Baricitinib is a drug for the treatment of rheumatoid arthritis, the evaluation of its use for the treatment of COVID-19 in pregnant women is discussed further (Taylor *et al*., 2017; Alzamora *et al*., 2020; Nana & Nelson-Piercy, 2021; Rasmussen & Jamieson, 2022; Schendrigin *et al*., 2022).

*Description and Pharmacological Effect of the Drug*

Baricitinib is an anti-inflammatory drug, a representative of the Janus kinase class, used in the treatment of rheumatoid arthritis. It blocks intracellular signaling pathways, which leads to the regulation of the synthesis of interleukins 2, 6, 10, and interferon-gamma. In observational studies, its use has been shown to be associated with a decrease in the mortality of patients with COVID-19. The mechanism of such a protective effect can be associated with both the anti-inflammatory effect of the drug and with a decrease in the penetration of the SARS-CoV2 virus into target cells (this effect was shown in an in vitro experiment). In addition, baricitinib normalizes the level of lymphocytes in patients with COVID-19 (Dashraath *et al*., 2020; Kalil *et al*., 2021; Maslova *et al*., 2021).

The use of baricitinib in healthy volunteers resulted in dose-dependent inhibition of STAT3 phosphorylation induced by IL-6, with maximum inhibition 2 hours after administration and a return to baseline after 24 hours. Within 1 week after the start of the use of baricitinib, the average absolute number of lymphocytes increased, but by the 24th week, it returned to its original value and subsequently remained stable for at least 104

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weeks. In most patients, the change in the number of lymphocytes was within the range of normal values. In patients with rheumatoid arthritis, a decrease in the concentration of serum C-reactive protein was observed as early as 1 week after the start of the use of baricitinib and remained reduced throughout the entire period of use (Alzamora *et al*., 2020; Schendrigin *et al*., 2022).

The use of baricitinib led to an increase in serum creatinine concentration by an average of 3.8 mmol / l after 2 weeks of treatment compared with placebo, in the future this indicator remained stable until the 104th week of treatment (Rasmussen, & Jamieson, 2022). This may be due to the inhibition of creatinine secretion by baricitinib in the renal tubules.

12 weeks after the start of the use of baricitinib, the average value of IgG, IgM, and IgA in the blood serum decreased and remained steadily reduced for at least 104 weeks. In most patients, the change in Ig values was within the range of normal values (Wallace *et al*., 2018; RECOVERY Collaborative Group, 2022).

*Treatment of Pregnant Women with COVID-19 in China*

When treating pregnant women infected with COVID-19, it is necessary to take into account many aspects that affect the health of a woman and her fetus, take into account physiological adaptation changes during pregnancy, as well as such a factor as the presence of an immunocompromised status in some women. Pregnant women may in many cases be more susceptible to COVID-19 infection than the general population. Due to the rapid spread of COVID-19 in the human body, the management of pregnant patients and ensuring the safety of the fetus are becoming serious problems. At the same time, there is quite a little information about the assessment of the health of infected pregnant women, and the potential risk of vertical infection of the fetus is unclear (Osipchuk *et al*., 2019; Alzamora *et al*., 2020; Wainstock *et al*., 2021).

New studies and descriptions of clinical cases of infected pregnant women report clinical features and obstetric and neonatal outcomes of pregnancy with pneumonia caused by COVID-19.

Seven pregnant women infected with COVID-19 were examined in Wuhan (China). Their symptoms from the onset of the disease were similar to those reported in non-pregnant adults with COVID-19. All patients received oxygen therapy and antiviral treatment in isolation. All the patients underwent cesarean section, as a result, the women and their fetuses were saved. Three newborns were tested for COVID-19, three had severe acute respiratory syndrome (SARS-CoV-2), and one was infected with COVID-19 36 hours after birth.

According to researchers and doctors who observed these women, five pregnant women were treated with hormonal drugs after cesarean section, and two of them additionally used methods of traditional Chinese medicine. However, there is no reliable data recommending any specific treatment for COVID-19 in pregnant women. WHO guidelines and some clinical data do not recommend the use of corticosteroids in COVID-19. The pool of medications used for the treatment of pregnant women should be based on reliable, proven data. It is necessary to conduct clinical trials to prove or disprove the effectiveness of certain drugs and treatment methods, as well as to investigate their effect on the fetus to develop a competent, standardized treatment for pregnant women infected with COVID-19 (Ghamri, 2022). Also, Chinese doctors continue to investigate the effectiveness of the treatment when applying the practices of Chinese traditional medicine.

The delivery time in this study ranged from 37 weeks to 41 weeks with an error of 5 days, almost all deliveries were performed by Caesarean section. In the case of pregnant women with COVID-19, there is currently insufficient data to determine exactly when a Caesarean section is necessary, and when natural childbirth is possible, more extensive practice is required. Previous treatment experience does not allow us to determine which method of delivery is safer among these patients (Jorgensen *et al*., 2020; Rossotti *et al*., 2020; Yang *et al*., 2020; Nana & Nelson-Piercy, 2021; Taylor *et al*., 2021; Durankuş & Aksu, 2022).

The following study reports nine pregnant women with COVID-19. Seven women gave birth to their children by cesarean section, and two by vaginal delivery. All newborns born vaginally (including two twins) had an Apgar score of at least 9 points and a negative test for nucleic acid (Pastick *et al*., 2020).

In these studies, all women were in the third trimester, and all had only mild symptoms. Consequently, the effect of SARS-CoV-2 infection on the fetus in the first or second trimester, or in patients with moderate or severe infection is unknown.

SARS infection during pregnancy can cause premature birth, intrauterine growth restriction, intrauterine death, and the death of a newborn (Rasmussen & Jamieson, 2022). Given that the probability and exact mechanisms that allow SARS-CoV-2 to cause severe obstetric and neonatal adverse outcomes are unknown, much more medical practice and data collection on such patients, as well as further studies, and careful screening of suspected cases during pregnancy, as well as long-term monitoring of mothers and their newborns are needed.

*Clinical Case of the Use of Baricitinib in the Treatment of Pregnant Women Infected with COVID-19*

**Figure 1** shows the frequency of various symptoms in pregnant women infected with COVID-19.

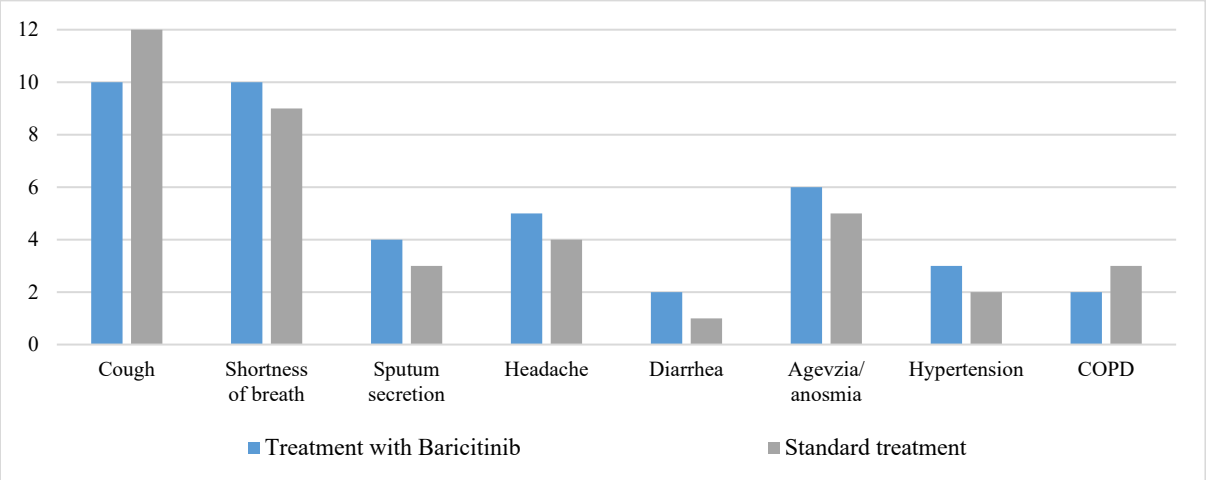


**Figure 1.** The presence of different symptoms in groups of infected pregnant women who received different treatments

Baricitinib is one of the inhibitors of cytokine release and is a promising anti-inflammatory drug. It is licensed for the treatment of rheumatoid arthritis (RA). This drug has good efficacy and safety indicators. There is information that this drug has an antiviral effect due to its interaction with one of the associated proteins, reducing endomitosis of SARS-CoV-2 (Taylor *et al*., 2017; Alzamora *et al*., 2020).

Based on this, it was decided to evaluate the efficacy and safety of baricitinib therapy in patients with COVID-19 of moderate severity. 34 patients aged 25 to 30 years with moderate severity of COVID-19 were hospitalized. The patients were divided into two groups, the control group (17 people) was offered standard treatment. The experimental group (17 people) was offered treatment with baricitinib (4 mg/day) in addition to the standard treatment method. The duration of treatment was 14 days (Şahin *et al*., 2021). **Table 1** shows some standard indicators of patients in both groups.

**Table 1.** Some standard indicators of two groups of patients

| Indicators | The experimental group that took Baricitinib | The control group receiving standard treatment | Probability value, P |
|---|---|---|---|
| Average body temperature | 38 | 38.1 | 0.356 |
| Respiratory rate, breaths/min | 23 | 22 | 0.665 |
| Oxygen saturation, % | 91 | 92 | 0.157 |
| PaO2/FiO2 | 290 | 268.6 | 0.603 |
| Heart rate, beats/min | 82 | 90 | 0.069 |
| Systolic pressure, mmHg | 120 | 105 | 0.003 |
| Diastolic pressure, mmHg | 70 | 62.5 | 0.094 |
| White blood cells, ($x10^9$/L) | 7.8 | 8.2 | 0.908 |
| Neutrophils ($x10^9$/l) | 6.5 | 6.9 | 0.707 |
| Lymphocytes ($x10^9$/l) | 0.7 | 0.89 | 1.000 |
| Hemoglobin (g/l) | 118 | 125 | 0.568 |
| Platelets ($x10^9$/l) | 203 | 366 | 0.000 |
| ALT (units/l) | 28.5 | 44 | 0.157 |
| AST (units/l) | 34 | 44 | 0.525 |
| Creatine (mg/dl.) | 1.00 | 1.00 | 0.583 |
| CRP, (mg/l) | 8.2 | 3 | 0.002 |
| Procalcitonin, (ng/mg) | 0.7 | 1.2 | 0.902 |

The intake of baricitinib took place in the form of tablets, orally. Tests for COVID-19 were taken using oral and nasal swabs. The criteria for evaluating patients included the presence of at least fever, cough, myalgia, and fatigue. After the course, patients treated with baricitinib were planned to be monitored for 6 months.

## Conclusion

Thus, the mechanisms of treatment of pregnant women in the presence of COVID-19 disease were considered. The approach to this issue of Chinese doctors who were the first to face this problem was considered, their experience and their clinical cases were examined, as well as the problems they had to face and methods of solving these problems.

A clinical case of the use of baricitinib in the treatment of infected pregnant women was examined. It is necessary to continue monitoring patients who have taken baracitinib in the treatment of COVID-19 to have a complete picture that allows us to conclude about the ineffectiveness or effectiveness of this treatment method, as well as to investigate the possible consequences that may occur from such a treatment method.

More research is needed to relate to the treatment of pregnant women with COVID-19 to make a more complete and holistic picture of the treatment of these patients, since pregnancy imposes certain restrictions on the use of drugs and treatment methods, and also increases the complexity of the clinical situation. It is necessary to take care not only of the health of the woman in labor but also of her child, as well as to monitor the child during the period after childbirth.

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