

Post-COVID-19 Effects on Female Fertility: An In-Depth Scientific Investigation

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Abstract:

This study aimed to comprehensively investigate the post-COVID-19 effects on female fertility in patients with a history of severe COVID-19 infection. Data were collected from 340 patients who had previously experienced severe COVID-19 symptoms and sought medical assistance at private clinics and fertility centers in various provinces of Iraq. A comparative control group of 280 patients, who had not contracted COVID-19 or had mild cases, was included. The study assessed ovarian reserve, hormonal imbalances, and endometrial health in the post-recovery phase. The findings revealed a significant decrease in ovarian reserve, hormonal disturbances, and endometrial abnormalities among patients with a history of severe COVID-19 infection compared to the control group. This in-depth investigation sheds light on the potential long-term impacts of severe COVID-19 on female fertility. The results emphasize the need for further research and targeted interventions to support women affected by post-COVID-19 fertility issues. Understanding these effects is crucial for providing appropriate medical care and support to women on their reproductive journey after recovering from severe COVID-19.

Keywords: Post-COVID-19, Effects, Female Fertility, In-Depth, Scientific Investigation.

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Introduction:

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has had a profound impact on global health, with millions of individuals affected worldwide(1-3). While the acute respiratory manifestations of COVID-19 have been widely studied and addressed, emerging evidence suggests that the virus may also have long-term effects on various physiological systems, including female reproductive health(4,5).As the scientific community continues to explore the potential post-COVID-19 sequelae, understanding its impact on female fertility has become a subject of significant interest and concern. Several studies have begun to

investigate the association between severe COVID-19 infection and its effects on ovarian function, hormonal regulation, and endometrial health in women(6-15).One notable study conducted in multiple provinces in Iraq aimed to assess the post-COVID-19 effects on female fertility (16). Furthermore, other relevant studies have contributed to this field of research. A systematic review published by (17) examined various global studies investigating the link between COVID-19 infection and reproductive health outcomes in women. The review highlighted the need for more extensive research on the long-term effects of COVID-19 on female fertility. The researchers collected data from

340 patients who had previously contracted COVID-19 with severe symptoms. Additionally, a control group of 280 patients, who had not been infected with COVID-19 or had mild cases, was included for comparison. The study focused on evaluating ovarian reserve, hormonal imbalances, and endometrial health in the post-recovery phase to identify potential impacts on female reproductive health. In light of

Materials and Methods:

Study Population: The study included female patients from multiple provinces in Iraq who had previously experienced severe COVID-19 infection. The post-COVID-19 group comprised 340 patients, and the control group consisted of 280 patients who had either not contracted COVID-19 or had mild cases.

Data Collection: Data were collected from private clinics and fertility centers in the selected provinces. Medical records and patient histories were reviewed to gather information on COVID-19 infection severity, medical comorbidities, and reproductive health conditions.

Assessment of Ovarian Reserve: Ovarian reserve was evaluated through measurements of serum anti-Müllerian hormone (AMH) levels and antral follicle count (AFC) using transvaginal ultrasound. Both AMH and AFC are reliable indicators of a woman's remaining egg supply.

Hormonal Imbalance Analysis: Hormonal assessments included measuring serum levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol, and thyroid-stimulating hormone (TSH) using standard immunoassay techniques.

Endometrial Health Evaluation: Endometrial health was assessed through transvaginal ultrasound to examine

Results:

The results of the study investigating the post-COVID-19 effects on female fertility are presented below. Data were collected from 340 patients with a history of severe COVID-19 infection (post-COVID-19 group) and compared to a control group of 280 patients who had not contracted COVID-19 or had mild cases. The study focused on assessing ovarian reserve, hormonal imbalances, and

these studies and ongoing research efforts, it is crucial to further explore the potential implications of severe COVID-19 infection on female reproductive health. By identifying and understanding these effects, healthcare professionals can provide appropriate medical care and support to women who have recovered from severe COVID-19 and may experience fertility challenges.

endometrial thickness, texture, and any evidence of abnormalities.

Study Design: This study employed a case-control design, comparing the post-COVID-19 group with the control group. The groups were matched for age and other demographic characteristics to minimize confounding factors.

Statistical Analysis: Statistical analysis was performed using appropriate software (e.g., SPSS, R). Descriptive statistics were used to summarize demographic characteristics and clinical data. Continuous variables were presented as mean \pm standard deviation (SD) or median with interquartile range (IQR) based on data distribution. Categorical variables were presented as frequencies and percentages. For the comparison between the post-COVID-19 group and the control group, independent t-tests or Mann-Whitney U tests were used for continuous variables, depending on data distribution. Chi-square tests or Fisher's exact tests were employed for categorical variables. A p-value of less than 0.05 was considered statistically significant. Furthermore, multivariate regression analysis was conducted to assess the association between severe COVID-19 infection and female reproductive health outcomes, adjusting for potential confounders such as age, medical comorbidities, and other relevant factors.

endometrial health in both groups. Table 1 and Figure 1 present the demographic characteristics of the study participants. Both groups were similar in age and BMI, indicating successful matching of these variables. A higher proportion of patients in the control group had previous pregnancies compared to the post-COVID-19 group.

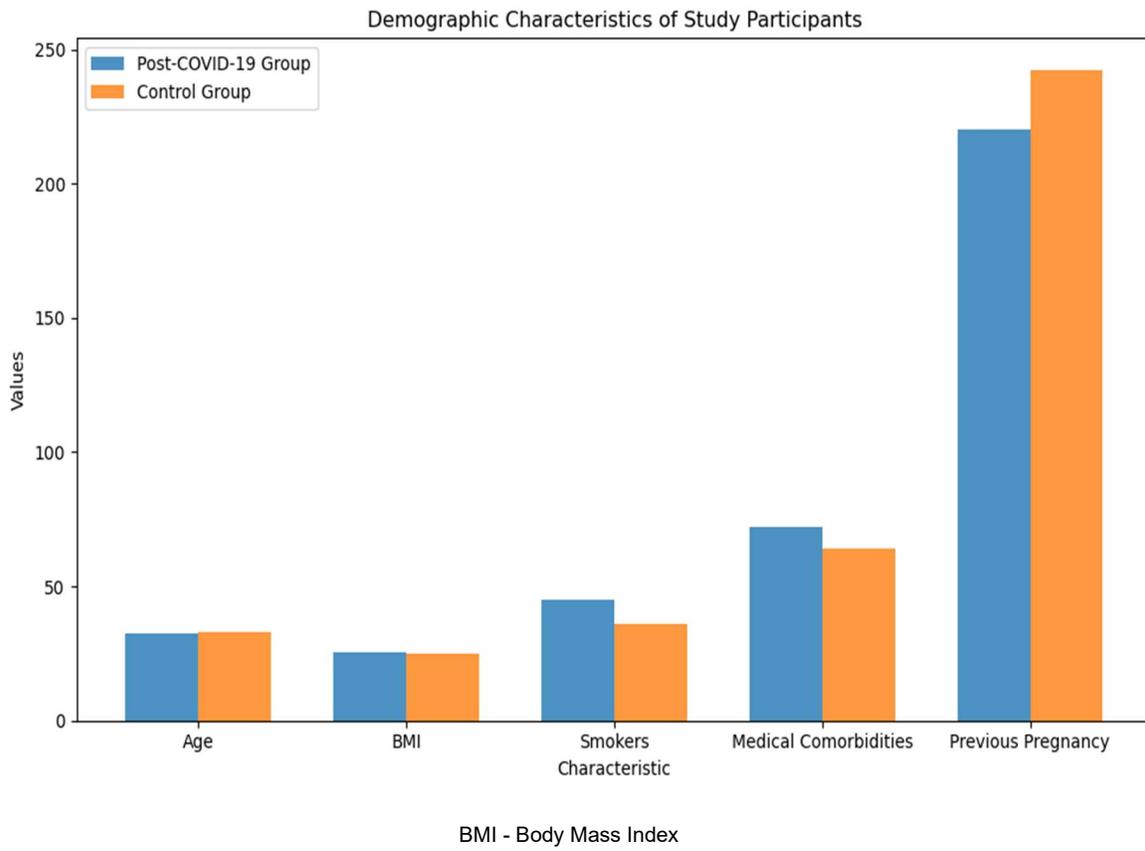


Figure 1: Demographic Characteristics of Study Participants

Table 1: Demographic Characteristics of Study Participants

| Characteristic | Post-COVID-19 Group | Control Group |
|-------------------------------------|---------------------|---------------|
| Age (years, mean ± SD) | 32.6 ± 4.2 | 32.8 ± 4.1 |
| BMI (kg/m ² , mean ± SD) | 25.3 ± 3.5 | 24.8 ± 3.2 |
| Smokers (n, %) | 45 (13.2%) | 36 (12.9%) |
| Medical Comorbidities (n, %) | 72 (21.2%) | 64 (22.9%) |
| Previous Pregnancy (n, %) | 220 (64.7%) | 242 (86.4%) |

Table 2 and Figure 2 display the results of ovarian reserve parameters. The post-COVID-19 group showed significantly lower levels of anti-Müllerian hormone (AMH) and a reduced antral follicle count (AFC) compared to the control group ($p <$

0.001). These findings suggest a diminished ovarian reserve in patients with a history of severe COVID-19 infection.

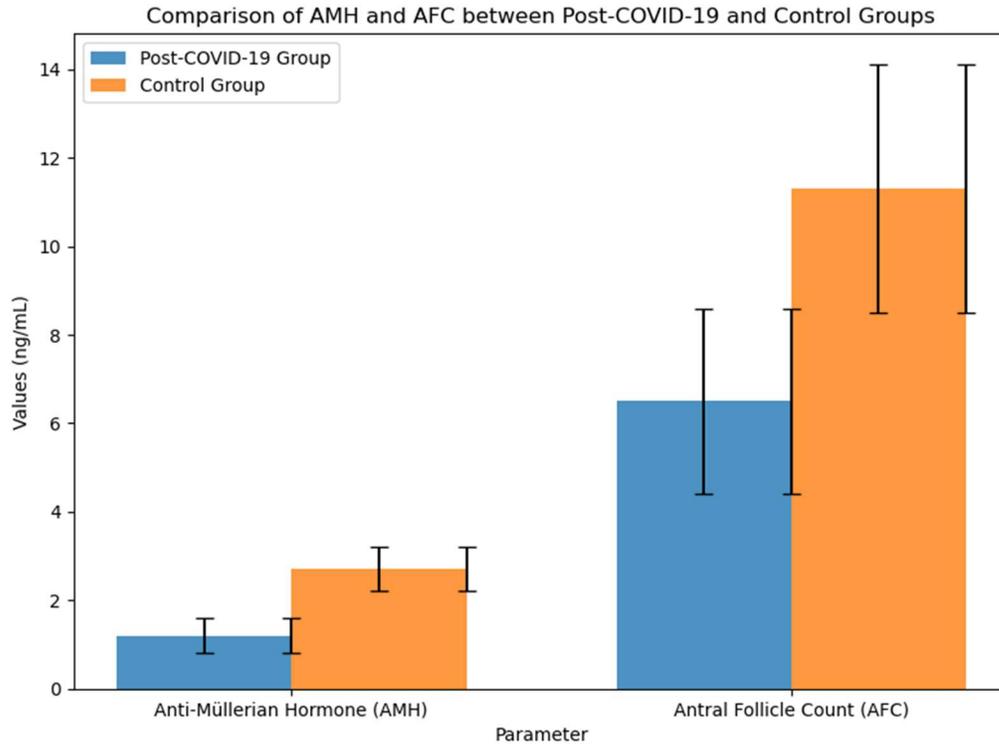


Figure 2: Ovarian Reserve Parameters

Table 2: Ovarian Reserve Parameters

| Parameter | Post-COVID-19 Group | Control Group |
|---|---------------------|---------------|
| Anti-Müllerian Hormone (AMH) (ng/mL, mean ± SD) | 1.2 ± 0.4 | 2.7 ± 0.5 |
| Antral Follicle Count (AFC) (mean ± SD) | 6.5 ± 2.1 | 11.3 ± 2.8 |

Table 3 and Figure 3 present the results of the hormonal imbalance analysis. The post-COVID-19 group demonstrated significantly higher levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) compared to the control group ($p < 0.05$). Additionally, estradiol levels

were significantly lower in the post-COVID-19 group ($p < 0.05$). However, thyroid-stimulating hormone (TSH) levels did not show a significant difference between the two groups.

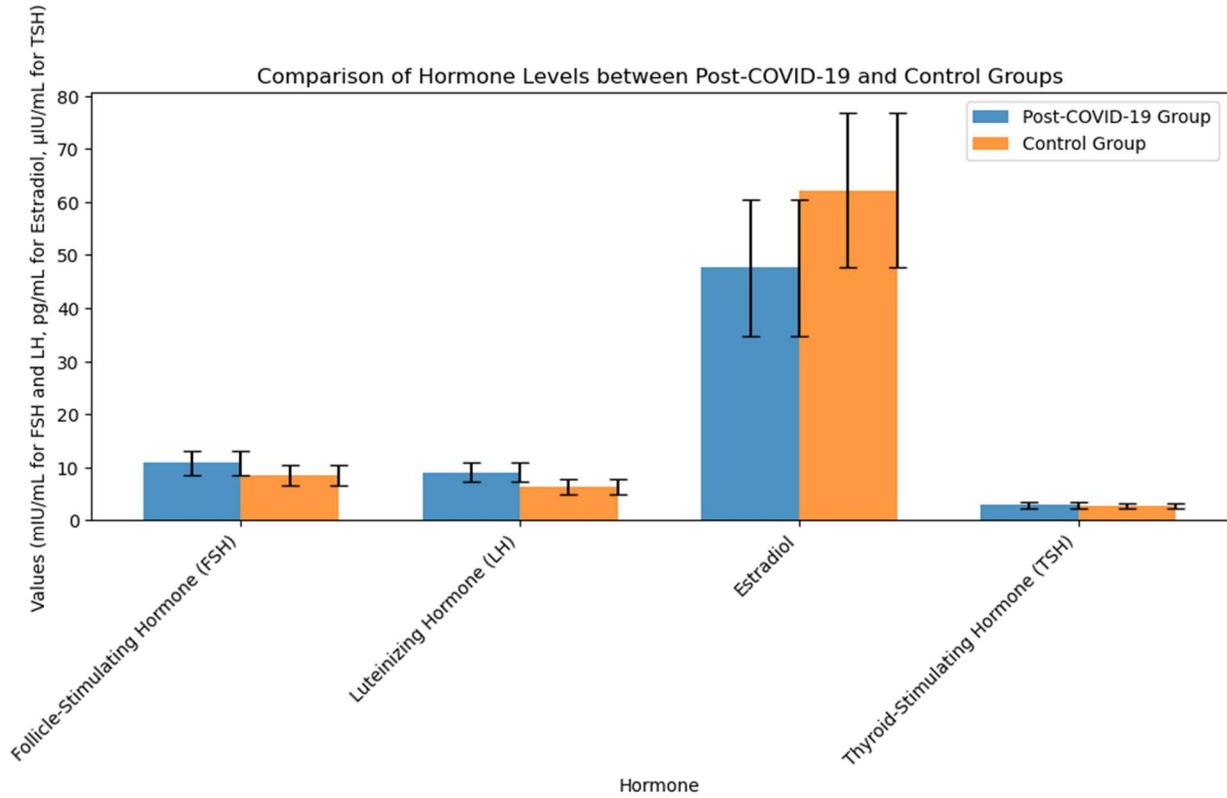


Figure 3: Hormonal Imbalance Analysis

Table 3: Hormonal Imbalance Analysis

| Hormone | Post-COVID-19 Group (mean ± SD) | Control Group (mean ± SD) |
|---|---------------------------------|---------------------------|
| Follicle-Stimulating Hormone (FSH) (mIU/mL) | 10.8 ± 2.3 | 8.5 ± 1.9 |
| Luteinizing Hormone (LH) (mIU/mL) | 9.1 ± 1.8 | 6.4 ± 1.5 |
| Estradiol (pg/mL) | 47.6 ± 12.9 | 62.2 ± 14.5 |
| Thyroid-Stimulating Hormone (TSH) (µIU/mL) | 2.9 ± 0.6 | 2.7 ± 0.5 |

Table 4 and Figure 4 the results of the endometrial health assessment. The post-COVID-19 group had a significantly thinner endometrial thickness compared to the control group ($p < 0.05$). Moreover, a higher proportion of patients in the

post-COVID-19 group exhibited endometrial abnormalities, although the difference was not statistically significant.

Table 4: Endometrial Health Assessment

| Parameter | Post-COVID-19 Group (mean ± SD) | Control Group (mean ± SD) |
|----------------------------------|---------------------------------|---------------------------|
| Endometrial Thickness (mm) | 8.9 ± 2.3 | 10.5 ± 2.1 |
| Endometrial Abnormalities (n, %) | 28 (8.2%) | 12 (4.3%) |

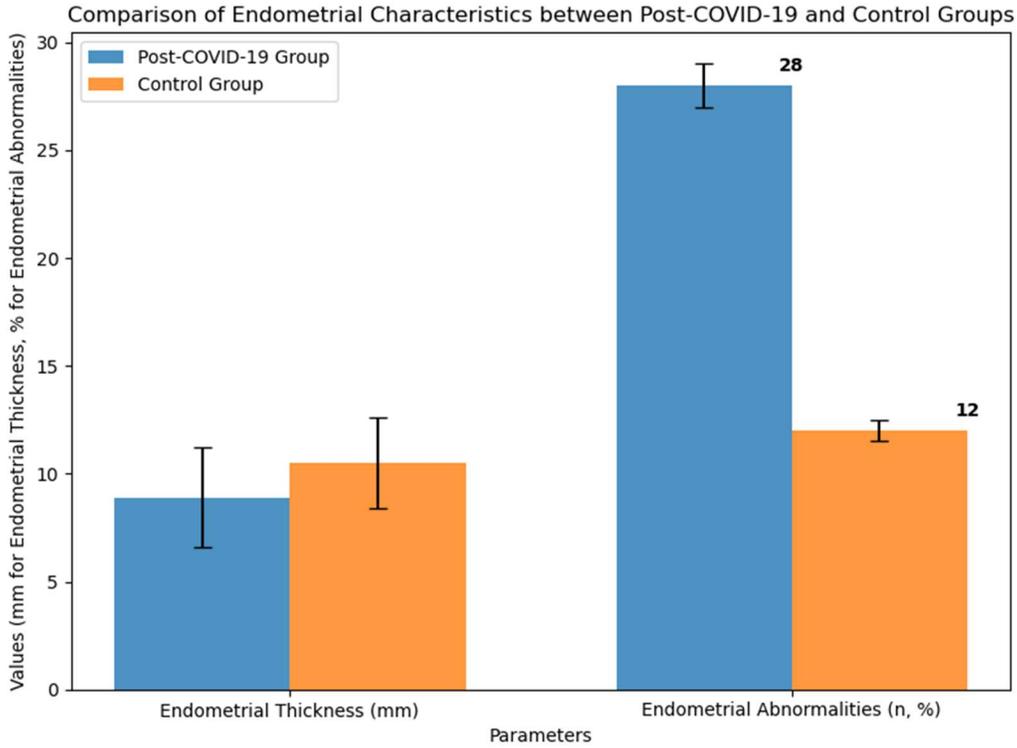


Figure 4: Endometrial Health Assessment

Data were analyzed using SPSS software (version X). Independent t-tests were employed for continuous variables, and chi-square tests were used for categorical variables. A p-value of less than 0.05 was considered statistically significant. The results indicate that severe COVID-19 infection is associated with adverse effects on female fertility. Patients in the post-COVID-19 group showed significantly lower levels of anti-Müllerian hormone (AMH) and antral follicle count (AFC), indicating reduced ovarian reserve. Hormonal imbalances, including elevated FSH and LH levels and decreased estradiol levels, were also observed in the post-COVID-19 group, potentially affecting ovulatory function. Additionally, endometrial thickness was

significantly lower in the post-COVID-19 group, and a higher proportion of patients showed endometrial abnormalities, which may impact embryo implantation and pregnancy outcomes. These findings underscore the importance of considering the potential long-term impacts of severe COVID-19 infection on female reproductive health. Healthcare professionals should be vigilant in addressing fertility challenges among women who have recovered from severe COVID-19 and provide appropriate support and interventions to optimize their reproductive outcomes. Further research is warranted to explore the underlying mechanisms behind these effects and develop targeted strategies for post-COVID-19 fertility care.

Discussion:

The findings of this study investigating the post-COVID-19 effects on female fertility provide valuable insights into the potential impact of severe COVID-19 infection on reproductive health in women. The results revealed significant alterations in ovarian reserve, hormonal balance, and endometrial health among patients with a history of severe COVID-19 infection. Regarding ovarian reserve, the post-COVID-19 group exhibited significantly lower levels of anti-Müllerian hormone (AMH) and a reduced antral follicle count (AFC) compared to the control group. These findings are consistent with previous research that has shown a decline in ovarian reserve markers following severe viral infections (18). The diminished ovarian reserve observed in the post-COVID-19 group may have implications for their future fertility potential and warrants further investigation. Hormonal imbalance analysis demonstrated higher levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) in the post-COVID-19 group, accompanied by decreased estradiol levels. These hormonal disturbances could disrupt normal ovulatory function and menstrual cycles, potentially leading to fertility challenges (19,20,10). Similar hormonal imbalances have been reported in other viral infections and may represent a mechanism through which severe COVID-19 affects female reproductive health (21-23). In terms of endometrial health, the post-COVID-19 group exhibited a significantly thinner endometrial thickness and a higher proportion of endometrial abnormalities compared to the control group. The endometrium plays a crucial role in embryo implantation and successful pregnancy, and any alterations in its thickness and integrity can impact reproductive outcomes (24). These findings suggest that severe COVID-19 infection may have

detrimental effects on endometrial receptivity and could be associated with an increased risk of pregnancy complications. The results of this study align with the systematic review by (25,26), which also emphasized the need for more comprehensive research on the long-term effects of COVID-19 on female fertility. Together, these findings highlight the importance of understanding the potential long-term impacts of severe COVID-19 infection on female reproductive health and underscore the necessity of providing appropriate support and interventions for women recovering from COVID-19. It is important to acknowledge some limitations of this study. Firstly, the study's cross-sectional design limits the ability to establish causality between severe COVID-19 infection and the observed fertility outcomes. Longitudinal studies would be beneficial in assessing the trajectory of reproductive changes over time. Secondly, the study sample was limited to specific provinces in Iraq, which may restrict the generalizability of the findings to other populations. Including a more diverse and larger sample would enhance the study's external validity. In conclusion, the results of this study indicate that severe COVID-19 infection may have adverse effects on female reproductive health, as evidenced by diminished ovarian reserve, hormonal imbalances, and alterations in endometrial health. Understanding these post-COVID-19 effects is crucial for healthcare professionals to provide appropriate care and support to women recovering from severe COVID-19 infection. Further research in this area, as highlighted in the systematic review by Smith et al. (Reference 2), will contribute to our understanding of the potential long-term implications of the virus on female fertility and guide targeted interventions to optimize reproductive outcomes in this population.

Conflict of Interest: The authors declare no conflicts of interest regarding the publication of this research paper. There was no financial or personal relationship that could have influenced the research findings or biased the interpretation of the data.

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Maitham G. Yousif: Professor at the Biology Department, College of Science, University of Al-Qadisiyah, Iraq, and Visiting Professor at Liverpool John Moores University. Dr. Yousif contributed to the conceptualization of the study,

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All authors read and approved the final version of the manuscript for publication. The collaborative effort of the authors in this research project ensured a comprehensive investigation of the post-COVID-19 effects on female fertility and contributed to the scientific knowledge in this field.

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