

# Factors Causing Maternal Death due to COVID-19 in Several Countries: A Literature Review

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## ABSTRACT

**Background:** Since 2019, the world has been faced with a global crisis. The spread of SARS-CoV-2 has an impact on all populations, including pregnant women, who are among the most vulnerable and at-risk population groups. The worldwide spread of the virus is called the COVID-19 pandemic. This study aims to explore the factors that cause maternal death during pregnancy and postpartum due to COVID-19 in several countries.

**Method:** A literature review was conducted to explore broadly the causes of maternal deaths due to COVID in several countries. Article search on three databases, namely PubMed, Google Scholar, and ScienceDirect. A total of 7 articles were analyzed. The data studied are cases of death and their causes.

**Results:** The study was conducted in the period 2018 to 2021 with the type of research using retrospective data. When compared to before the pandemic, there was a significant increase in the number of maternal deaths. Factors that increase the risk of maternal death come from direct and indirect factors. Indirect factors such as age, health facility access, inadequate tools, and health services, access to knowledge, cultural practice, and poverty. Direct factors are comorbidities such as obesity, diabetes, cardiovascular disease, hypertension, and immune impairment. Pregnant women who do not have comorbidities can have a poor prognosis with undetected causes of death. Health facilities need to conduct early screening so that direct and indirect factors can be minimized to prevent maternal mortality.

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## INTRODUCTION

COVID-19 emerged in December 2019 which caused the world to be faced with a global crisis. The cause of the pandemic is Severe Acute Respiratory Syndrome Coronavirus 2 (SARS CoV-2). Symptoms that appear are some general symptoms such as fever, muscle aches, and respiratory problems.<sup>1</sup> Not only that, but this virus also has the potential to cause high levels of illness and death in millions of people<sup>2</sup>. This morbidity and mortality rate also includes maternal mortality.<sup>3</sup>

Reducing the global maternal mortality ratio to less than 70 per 100,000 live births is one of the targets of the Sustainable Development Goals (SDGs). MMR is one indicator of the success of development in the health sector and describes the quality of maternal health.<sup>4</sup> However, efforts to achieve targets following the Sustainable Development Goals (SDGs) have been hampered due to COVID-19. Pregnant women are considered to be among the most vulnerable and at-risk populations in dealing with the spread of this virus.<sup>5</sup> Even

though pregnant women have been at risk and have been dealing with types of diseases since before the pandemic.<sup>6</sup>

During the pandemic, maternal death rates increased considerably in all nations around the world. According to multiple studies, a substantial proportion of pregnant and postpartum women performing COVID-19 were hospitalized. This increase in cases remained throughout the second wave, as did the number of maternal deaths caused by COVID-19.<sup>2</sup> Pregnant women who die from COVID-19 account for 25% of the general population in the United States, and 33% require assistance with breathing equipment such as ventilators. In the case of Wuhan, China, for example, a study was carried out on 9 third-trimester pregnant women with symptoms of COVID-19 viral pneumonia who had a 33% morbidity rate.<sup>7</sup> In contrast to lower-middle-income nations like Brazil, 978 pregnant and postpartum women with COVID-19 reported a total of 124 deaths in June 2020. This indicates that this particular incident has a

fatality rate of 12.7%.<sup>8</sup> In Iran, 7 out of 9 second and third-trimester pregnant women die, 1 out of 9 is still severely ill and requires a ventilator, and the remaining 1 out of 9 has recovered after spending long periods in the hospital.<sup>7</sup>

According to studies from the United States, pregnant women who are infected with COVID-19 and develop symptoms are more quickly referred to the ICU and require further treatment.<sup>9</sup> Previous research also stated that the number of maternal deaths due to COVID-19 was still relatively low in the first wave, but in the second wave, both pregnant and postpartum women from various countries experienced symptoms that were much more severe and deadly, which was linked to the emergence of variants new strains of the SARS-Cov-2 virus. The presence or absence of a history of previous comorbidities in the mother also influences the Maternal Mortality Rate (MMR).<sup>2</sup>

The Maternal Mortality Rate (MMR) during the pandemic needs to be a separate focus for a deeper study of the causative factors and what prevention can be done as early as possible.<sup>10</sup> At the time of the pandemic, there was a data bias between maternal deaths caused purely by COVID-19, and COVID-19 as an aggravating disease and other diseases. Factors causing death due to exposure to COVID-19 in pregnant women need to be studied to differentiate and prevent complications.<sup>4</sup>

Various countries are facing a similar problem, namely COVID-19. Data on maternal mortality due to COVID-19 around the world varies with possible different causes due to different capacities of health systems. A thorough examination of maternal deaths due

to COVID will help identify gaps and weaknesses in the awareness of risk factors and proper treatment, minimizing maternal mortality rates. This study aims to explore the causes of maternal death due to COVID-19 in several countries. This is to support the evaluation so that exposure to COVID-19 does not exacerbate the risk of maternal death. Information about maternal mortality will have an impact on improving reproductive health, especially pregnancy services, and realizing making pregnancy safer in the community, especially for mothers and families.

### METHOD

A literature review was carried out to look more broadly at the causes of maternal death due to COVID-19 in several countries. The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guide is used for study preparation. A total of 3 databases namely PubMed, Google Scholar, and ScienceDirect were accessed to find relevant studies. A combination of the terms Medical Subject Heading (MeSH) namely: 'maternal death', 'pregnancy', 'postpartum period', 'COVID-19', and 'SARS-CoV-2' were used as keywords. In addition, Boolean Operators, such as AND, OR, and NOT, were also used in the search. This research only included selected studies, namely quantitative studies, using English, research objectives according to the issues raised, open access articles, and published in 2017-2022. Other types of research such as letters to the editor, case reports, animal experimental research, critical appraisal, and abstracts without full articles were excluded from this study.

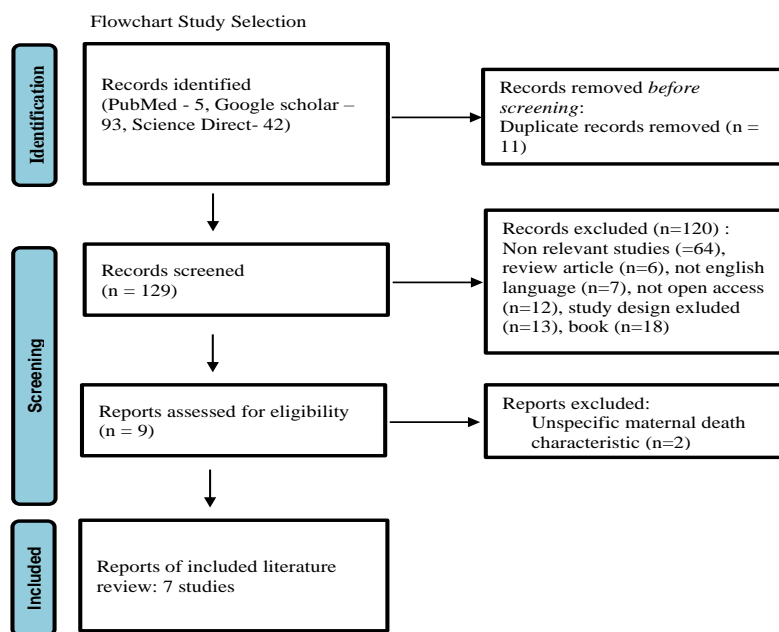


Figure 1. Prisma flow research

Microsoft Excel is used to write down the title and abstract of the search results. The title is then filtered and selected. The articles were selected based on the agreement between the authors. If there is no agreement, external collaborators was consulted. The authors assess the quality of articles using existing tools. The Center of Evidence-Based Medicine (CEBMA) was used to assess cross-sectional type studies. The Critical Appraisal Skills Program (CASP) was used to assess case-control and cohort-type studies. These tools are used to criticize or evaluate research evidence and whether there is bias in the planning, implementation, and analysis.

The analysis was carried out based on research results and recommendations found in each study. The results were synthesized in a table of study characteristics and findings. The meaning of the research results found is then drawn into conclusions. Table 4 presents the authors, year, country, study design, data collection, sample, mortality, and characteristics of the deaths.

## RESULTS AND DISCUSSION

The initial search found about 140 articles in 3 databases. 129 articles indicated relevance based on the abstract, year, and language. A total of 9 studies were accessed and rated using critical appraisal tools, but 2 studies did not

specifically describe the characteristics of maternal mortality. 7 articles were analyzed in this review. Data was obtained from secondary data, namely maternal mortality, COVID-19 registers, and surveillance data. The PRISMA flow chart is presented in Figure 1. The articles analyzed have moderate category quality and are presented in Table 1, Table 2, and Table 3.

The results of this study indicated that there is an increase in the number of maternal and postpartum deaths when compared to before the pandemic. The presence of physiological immunosuppression is a feature of pregnancy, making this population more susceptible to viral infections and pathogens in the respiratory system.<sup>11</sup> Exposure of pregnant women to COVID-19 can affect the Maternal Mortality Rate (MMR). The high number of MMR in several regions around the world can hinder the development of the country and social economy. Based on data from the Directorate of Family Health, 1,086 mothers died as of September 14, 2021, due to COVID-19.<sup>4</sup> Factors that increase the risk of maternal death come from direct and indirect factors. Indirect factors such as age, health facility access, inadequate tools, and health services, access to knowledge, cultural practice, and poverty. Before the pandemic, these indirect factors also had an influence. Policies and strategies need to be carried out by the government, especially leading observers of maternal health, including the United Nations.

**Table 1.** Article quality assessment for cross-sectional design study using Centre of Evidence-Based Medicine (CEBM) appraisal tools

Author, year	Did the study focus question /issue?	Is the research method appropriate for answering the research question?	Is the method of selection of the subjects clearly, described?	Could the sample selection introduce bias?	Was the sample representative regarding the population?	Was the sample size based on pre-study considerations of statistical power?	Was a satisfactory response rate achieved?	Are the measurements likely to be valid and reliable?	Was the statistical significance assessed?	Are confidence intervals given for the main results?	Could there be confounding factors that have not been accounted for?	Can the results be applied to your organization?	Quality
Fatmaningrum (2022)	Y	Y	Y	C	Y	Y	Y	Y	Y	Y	Y	Y	M
Basu (2021)	Y	Y	Y	Y	C	Y	Y	Y	Y	N	Y	Y	M

Notes: Y = yes, C= can't tell, N = No, M= moderate overall quality, L = low overall quality

**Table 2.** Article quality assessment for case-control study using Critical Appraisal Skills Programme (CASP) tools

Author, year	Did the study address a focused issue?	Did the authors use an appropriate method to answer their question?	Were the cases recruited in an acceptable way?	Were the controls selected in an acceptable way?	Was the exposure accurately measured to minimize bias?	Aside from the experimental intervention, were the groups treated equally?	Have the authors taken account of the potential confounding factors in the design and/or in their analysis?	How large was the treatment effect?	How precise was the estimate of the treatment effect?	Do you believe the results?	Can the results be applied to the local population?	Do the results of this study fit with other available evidence?	Quality
Thakur (2022)	Y	Y	Y	Y	C	N	C	Y	Y	Y	Y	Y	M
Mendez-Dominguez (2021)	Y	Y	Y	Y	Y	N	N	Y	C	Y	Y	Y	M
Thoma & Declercq (2022)	Y	Y	Y	Y	Y	Y	C	Y	Y	Y	C	Y	M
Daclin (2022)	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	C	Y	M

Notes: Y = yes, C= can't tell, N = No, M= moderate overall quality, L = low overall quality

**Table 3.** Article quality assessment for cohort study using Critical Appraisal Skills Programme (CASP) tools

Author, year	Did the study address a focused issue?	Was the cohort recruited acceptably?	Was the exposure accurately measured to minimize bias?	Was the outcome accurately measured to minimize bias?	Have the authors identified all-important confounding factors?	Have they taken account of the confounding factors in the design and/or analysis?	Was the follow-up of subjects complete enough?	Was the follow-up of subjects long enough?	What are the results of this study?	How precise are the results?	Do you believe the results?	Can the results be applied to the local population?	Do the results of this study fit with other available evidence?	What are the implications of this study for practice?	Quality
Hojo-Souza (2022)	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	C	M

Notes: Y = yes, C= can't tell, N = No, M= moderate overall quality, L = low overall quality

**Table 4.** Description of research article included

<b>Author, Year</b>	<b>Country</b>	<b>Study Design</b>	<b>Data Collection Date</b>	<b>Sample</b>	<b>Mortality Rate</b>	<b>Death Characteristics</b>
Fatmaningrum (2022) <sup>4</sup>	East Java, Indonesia	Cross-sectional	January 1, 2019-December 31, 2020	Data on maternal mortality from the East Java Provincial Health Office	The number of Maternal deaths in 2019 was 520 deaths, in 2020 was 565 deaths,	Age more than 35 years old, gravida, distance, inadequate service, poverty, lack of information, cultural practice, rescue relay
Thakur, (2022) <sup>12</sup>	India	Case-control	Data from 2019-2020	Data obtained from the Department of Obstetrics and Gynecology, Institute of Postgraduate Medical Education and Research (PGIMER), Chandigarh	There was an increase of 45.6% to 52.5% of cases of maternal deaths with direct causes during the COVID-19 pandemic in the first two years. There was a decrease in cases of maternal death with indirect causes from 38.2% to 25.4%. Patients who died increased from 5.9% in 2019 to 11.9% in 2020.	Pregnant women with ARDS, lack of information, lack of financial resources
Mendez-Dominguez, (2021) <sup>13</sup>	Mexico	Case-control	February 28, 2020, to February 28, 2021	Surveillance data from General Office of Health Information	MMR increased by 56.8%, confirmed COVID-19 22,93%, and 4,5% unconfirmed case	Pregnant women with ARDS, smoking and cardiovascular disease. Age <19 or > 38 years old. Pneumonia, Asthma, immune impairment, diabetes and increased BMI can increase the mortality risk.
Thoma M (2022) <sup>14</sup>	US	Case-control	Data from 2018 - 2020	NCHS mortality and natality files	There was an increase from 18.8 per 100,000 live births to 25.1 per 100,000 live births in cases of maternal death. This figure increased by 33.3% after March 2020. Final maternal mortality increased to 41%	About 56.9% of maternal deaths are caused by indirect causes. This cause is COVID-19 or conditions made worse by COVID-19 or other health care disorders (diabetes or cardiovascular)
Basu (2021) <sup>15</sup>	Africa-South Africa	Cross-sectional	April – September 2020	COVID registers and maternity case records	103 pregnant women were confirmed COVID, and 6 from it died.	Mean Age 33,5, multiparous, Mean Gestational Age was 35 weeks, Comorbid - Hypertension, DM, HIV, dyspnea, high lactic dehydrogenase, macerated stillborn.

Daclin, (2022) <sup>16</sup>	France	Case control	March 2020 - February 2021	Cases: all pregnant women tested positive for COVID-19 in March 2020 and February 2021 Control: pregnant women who gave birth in a row in September 2019, when the disease COVID-19 had not yet appeared in France	About 5.8% of the 86 patients infected with the virus required hospitalization. Approximately 1.2% were admitted to the ICU and there was no indication of severity. The risk of maternal death is 1.6% in a multinational cohort study	Obesity, comorbid: gestasional diabetes
Hojo-Souza, (2022) <sup>2</sup>	Brazil	Cohort	Patients with confirmed initial symptoms of COVID-19 between the epidemiological weeks (EW) of 2020-8 and 2021-15.	Data collected from the Influenza Epidemiological Surveillance Information System (SIVEP-Gripe)	Maternal and postpartum deaths from COVID-19 increased dramatically in the second wave in Brazilian hospitals. The results of the hCFR analysis showed a significant increase in both pregnant and postpartum women.	Comorbid: dyspnoea, respiratory distress, cardiac disease, diabetes, maternal obesity; lower access and availability of healthcare, low-middle socioeconomic.

Organizations focus less on indirect causes of maternal death, except HIV infection. Main attention is still paid to the direct causes of adverse pregnancy outcomes.<sup>17</sup> The proportion of maternal deaths due to indirect medical causes has increased in low to middle-income countries.<sup>18</sup>

In addition to indirect factors, direct factors play an important role in maternal mortality due to COVID-19. Direct factors are comorbidities such as obesity, diabetes, cardiovascular disease, hypertension, and immune impairment. Pregnant women who do not have comorbidities can have a poor prognosis with undetected causes of death. This indicates the need for early internal disease examination. Since before the pandemic, Cardiovascular Diseases (CVD) is the leading cause of death during pregnancy. Therefore, its early detection in pregnancy is of great importance.<sup>19</sup> The description of the included studies is presented in Table 4.

**Individual Factors**

Socio-demographic factors are individual factors that can influence the high mortality rate of pregnant women due to COVID-19, such as age, gravida, comorbidities, and knowledge.<sup>20</sup> Age is a contributing factor to maternal mortality

due to COVID-19. In Indonesia, over 35 years of age increases the risk of death. In Mexico, it was stated that the maternal mortality rate during the pandemic occurred at the age of < 19 years and age > 38 years. Meanwhile, in South Africa, the average age of pregnant women who experience COVID is 33.5. India also includes age as an indirect factor that increases the risk of maternal death.<sup>13</sup>

Gravida is also mentioned as a factor that can affect the severity of the COVID-19 infection experienced by mothers, this is mentioned in Indonesia and South Africa. In the journal of Basu (2021), it is stated that the majority (83%) of pregnant women who suffer from COVID are multiparous. Maternal mortality due to gravida usually occurs in pregnant women with gravida 2 or 3. In 2019-2020, in Indonesia, there is an increase in mortality in multiparous mothers.<sup>15</sup>

Individual factors have less significance in industrialized countries. People in industrialized countries, such as France, have high health awareness. Daclin's research (2022) was carried out at the Obstetrical Department of Foch Hospital, located in West Parisian, which has a middle-high socioeconomic level. Most of them are cautious about their health and have financial resources to care for their health. The West Parisian neighborhood also has an excellent healthcare system.<sup>16</sup>

### **Health Facilities**

Indirect factors also affect such as limited access to health facilities which also causes treatment not to be optimal. Not all hospitals have adequate facilities to provide treatment for pregnant women with COVID which is highly severe. The lack of information related to referrals also makes pregnant women with COVID come late to health services. Cultural practices that still occur in the community also affect the delay in mothers being referred to health services.<sup>2</sup> Access to health services is relatively strong in countries with higher incomes such as the United States and France, but this is not the case in low-middle-income countries, where access to health is still varied and limited.<sup>16</sup>

During the pandemic there were many problems in health access related to policies due to COVID-19 most countries are in lockdown. This is also the case in England. Inequality in access to health occurred as a result of the UK government's lockdown policy during the COVID-19 pandemic, which affected mostly women, ethnic minorities, and those with chronic diseases.<sup>21</sup> Compared to before the pandemic, there has been a decrease in accessibility to health services during the COVID-19 pandemic. This decline is described in terms of decreased surgical plans, doctor appointments, admissions to the hospital or ED, and access to drugs.<sup>22</sup> During the COVID-19 lockdown, a large proportion of chronic care patients experienced barriers to accessing healthcare<sup>23</sup>

During the COVID-19 pandemic, there were problems with access to antenatal care, even though this service is important for detecting abnormalities and complications for pregnant women. This situation causes pregnant women to experience delays in health services, although there is no definitive data on severe delays due to fear of a pandemic.<sup>24</sup> The lockdown situation has caused restrictions on interaction with health professionals in the ANC and delivery processes. This also results in their partners not being able to attend antenatal appointments or support them in the postpartum period in the maternity environment. The lack of information about COVID-19 and pregnancy makes women even more unsure about pregnancy and childbirth.<sup>25</sup> There is a real threat to health posed by COVID-19, disrupting their plans to conceive and give birth, further adding to the risk to their health and well-being.<sup>26</sup>

### **Comorbid**

Concomitant disease factors greatly affect the severity of the condition of pregnant women suffering from COVID-19. Patients with comorbidities have a higher risk of death than those without comorbidities. The comorbid referred to based on reviews from several

countries are mentioned as heart disease, hypertension, diabetes, asthma, ARDS, pneumonia, obesity, HIV, and autoimmune diseases.<sup>13</sup> According to Daclin's findings, the rate of obese mothers in West Parisian is quite high when compared to other populations. Obese pregnant women are more likely to suffer severe COVID-19 symptoms than non-obese pregnant women. Pregnant women will enter the ICU if they experience COVID-19 with a poor prognosis.<sup>16</sup> Obesity contributes to severity by impairing type I and III interferon responses and altering the suppressors of cytokine signaling. This situation can prevent cleaning the virus. The systemic immune system suffers from chronic inflammation caused by obesity. Death in patients with acute respiratory distress syndrome occurs preceded by the release of pro-inflammatory lipid leptin, and high levels of leptin in the bloodstream. Impaired pulmonary function is a combined consequence of obesity-related delays in COVID-19 immune regulation, mechanical stress, and increased adipose tissue.<sup>27</sup>

### **Women Perception**

The attitude and risk perception of pregnant women toward the COVID-19 pandemic were low. Pregnant women's awareness, ANC, and risk perception were all significantly related to their attitude toward the COVID-19 pandemic<sup>28</sup>. This is clearly stated in the results of research from the state journals of Mexico, the US, and South Africa. In dealing with chronic diseases, women's behavior and involvement related to pregnancy need to be improved. Their perception of health services appears to be influenced by their perception of the risk of pregnancy due to chronic disease itself. Women with chronic diseases have very individual risk perceptions. Women's pregnancy risk assessment and communication should take into account their understanding and perception of risk<sup>29</sup>. Chronic disease prevalence in the mother during pregnancy has increased. This needs to be watched out for because based on research there was an increased risk in the period 2009 to 2013, compared to 1989 to 1993<sup>30</sup>. Nevertheless, pregnant women who do not have comorbidities can have a poor prognosis with undetected causes of death, so the monitoring of pregnant women who suffer from COVID even without comorbidities must be carried out strictly.

This study's limitation is that it only describes the situation in several countries and has not described how these countries have responded to this case. Further research needs to explore programs carried out by countries to address the increasing maternal mortality rate and examine effective solutions. This can prevent similar incidents in the future.

## CONCLUSION

There is an increase in the number of maternal deaths when compared to before the pandemic. Factors that increase the risk of maternal death come from direct and indirect factors. Indirect factors such as age, health facility access, inadequate tools, and health services, access to knowledge, cultural practice, and poverty. Direct factors are comorbidities such as obesity, diabetes, cardiovascular disease, hypertension, and immune impairment. Countries need to address and prevent severity in mothers with COVID by increasing access to and early detection of the disease. Further research needs to explore programs carried out by countries to address the increasing maternal mortality rate and examine effective solutions.

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