GIVING BIRTH BY CAESAREAN SECTION IN WOMEN INFECTED WITH COVID-19 AND THE INCIDENCE OF COVID-19 IN NEWBORN: A SYSTEMATIC REVIEW

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ABSTRACT

Labor method by caesarean section in Covid-19 infected pregnant women had higher ratio than vaginal delivery. The use of Caesarean section is adjusted to the condition of the mother or/and the baby. However, the literature on labor method and its relation to Covid-19 infection in newborn is rare. We conducted a review about association between giving birth by caesarean section in women infected with Covid-19 and the incidence of Covid-19 in the newborn. This research was an analytic systematic review and guided by PICO. Studies from NCBI and ScienceDirect were used to locate full text articles, written in English, published from 2019-2021. The search strategy included terms for (Cesarean Section or Delivery, Obstetric) and (Covid-19 or Sars-Cov-2) and infant, newborn and infectious disease vertical transmission. Articles were included when met the inclusion and exclusion criteria, then analysed with RevMan 5.4. The search yielded 205 records. After full text screening, 3 studies were found to meet all criteria and 3 studies were obtained from manual search. Six studies using cohort designs were based in the United States, China, Morocco, Spain, and Turkey. Sample sizes ranged from 15 to 125 participants. Overall effect z=0.81 (p value=0.42) showed that the caesarean section had no significant protective factor from Covid-19 infection in newborn. Our finding indicated that babies who were born from mothers with Covid-19 infection. However, there was possible publication bias and samples collected were minimum. More studies are needed to advance this emerging literature.

ARTICLE HISTORY

Received: December, 13, 2022
Revision: February, 14, 2023
Accepted: March, 07, 2023
Online: June, 12, 2023

doi:
10.20473/jcmphr.v4i1.45121

KEYWORDS
Caesarean section, Communicable disease, Covid-19, Obstetric, Pregnant

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How to cite:
Umiastuti, P., Mahardika, N.P., Nisa, A.I., Suropati, M.B., Hasanah, R. U., Prasasta, R.E.D., Fairuz., J.J., Kalishah, J., Giving Birth by Caesarean Section in Women Infected with Covid-19 and The Incidence of Covid-19 in Newborn. Journal of Community Medicine and Public Health Research, 4(1): 55-64.

INTRODUCTION

Childbirth method is divided into two, normal delivery and caesarean section. Normal delivery is expelling the fetus at term (37-42 weeks) and the fetus is born spontaneously with a back-of-the-head presentation that takes place within 18 hours without maternal or fetal complications[1-2]. Caesarean section (SC) is the birth of the fetus through an incision in the abdominal wall (laparotomy) and uterine wall (hysterotomy)[3].

Based on the 2017 Indonesian Demographic and Health survey results, Indonesia's caesarean section delivery rate was 17.02%[4]. However, this survey was followed by the unequal use of caesarean delivery, where 66.5% of caesarean section deliveries were carried out by urban women and 75% of caesarean section deliveries were carried out by middle- and upper-class women[5]. Almost all provinces in Indonesia have rates above 10%. There were no exact data regarding the number of normal deliveries related to economic conditions, the environment, and the condition of the pregnant women[6].

The coronavirus disease 2019 (Covid-19) presented a new challenge to the team working in the healthcare system, including the treatment of patients, particularly in the obstetrics and gynecology area[7-8]. Regarding the mode of delivery, a high rate of cesarean sections (C-sections) was observed in patients infected with SARS-CoV-2 in the early phases of the pandemic. A C-section is a mode of delivery through laparotomy and hysterotomy before the removal of the fetus begins. It requires anesthesia and follow-up care[9-10]. Among pregnant women who tested positive for Covid-19, around 64% gave birth through cesarean section, with this percentage reaching 93% in China[11].

According to data in Indonesia, in a pregnancy, the third trimester is the most vulnerable time for the Covid-19 virus. Fetal complications in women infected with Covid-19 include miscarriage (2%), Intra Uterine Growth Restriction (IUGR) (10%), and premature birth (39%)[12]. The mode of delivery is determined by obstetric factors and clinical urgency. Since there is no conclusive evidence of vertical transmission, vaginal delivery is not contraindicated in patients with Covid-19[13]. However, caesarean section is chosen for pregnant woman who has respiratory problems[13].

Pregnant women with Covid-19 virus infection have a risk of complications for the baby they are carrying. The most cases are premature births and the use of the caesarean section method for the benefit of the woman who have respiratory function disorders. There is no clear evidence of vertical transmission from mother to baby through vaginal delivery or a reduced risk of mother-to-child transmission of Covid-19 through caesarean section. Therefore thereis a need to do a systematic review to determine the association between giving birth by caesarean section in women infected with Covid-19 and the incidence of Covid-19 in newborn to help health providers taking better decisions for patients with related condition.

MATERIALS AND METHODS

Research Method

This research was analytic systematic review. It aimed at identifying, assessing, and interpreting all findings on a

research topic and to answer predefined research questions. This research was conducted at the Department of Public Health and Preventive Medicine of the Faculty of Medicine, Universitas Airlangga, Surabaya in May 2021. The criteria for searching for research literature using the PICO (Population, Intervention, Comparison, and Outcome) method are presented in Table 1. Characteristics of the population are pregnant women infected with Covid-19 worldwide with intervention for delivery via caesarean section, vaginal delivery, and the incidence of newborns infected with Covid-19.

Table 1. PICO formula

Characteristics of PICO	Search Terms
Population	Pregnant women suspected and infected with Covid-19
Intervention	Caesarean section delivery
Control	Vaginal delivery
Outcome	The incidence of newborns infected with Covid-19

The population was pregnant women confirmed and suspected with Covid-19 worldwide. The sample involved pregnant women with confirmed Covid-19 infection in Saudi Arabia, Iran, Turkey, United States, United Kingdom, China and Spain. The inclusion criteria were English journals, caesarean section intervention, outcome of decreasing the incidence of newborns infected with Covid-19, pregnant women infected with Covid-19 at the third trimester of pregnancy, type of publication of original articles with full text, study design of case control, cohort or randomized controlled trial (RCT), the year of publication between 2019-2021. Meanwhile, the research exclusion criteria included articles with titles that were not related to childbirth and Covid-19 infection, articles with descriptive studieswhose OR values could not be determined, and research samples of pregnant women or infants who did not use the RT-PCR serological method.

Literature searches were carried out in databases (PubMed) and (ScienceDirect) by selecting journals based on the year of publication from 2019 to 2021. Additional studies were included by manual search. Search for articles or journals using keywords and boolean operators (AND, OR NOT or AND NOT) to expand or narrow the search, making it easier to search and to determine the use of articles or journals. The keywords in this systematic review consisted of (Caesarean section OR Delivery, Obstetric) AND (Covid-19 OR SARS-CoV-2) AND Infant, Newborn AND Infectious Disease Transmission, Vertical. The colleted data were managed using the PICO (Population, Intervention, Comparison, and Outcome) method. All articles collected were processed using identification, screening, eligibility, and include to sort the inclusion and exclusion characteristics of the articles obtained accordingly.

The analytical method in this systematic review was based on topics that had been determined in the systematic review to describe and explain the research results narratively. Relevant data were examined by review questions: author, country, year, background, theoretical framework, research objectives, conceptualization of cultural competence, educational content, research design, sample size, sampling method, participant description, reliability and validity, measurement instrument,

statistical analysis and techniques, results related to cultural competence, and analysis of results. The narrative approach has the main objective of gathering evidence on the effectiveness of interventions and developing a coherent textual narrative.

Research Selection

As many as 205 articles were found through identification and none of them were duplicated (n=0). The documents that had been identified were screened to omit excluded documents (n=150) so that documents that meet the requirements were obtained (n=55). Among the 55 studies, 52 were not taken because the titles and abstracts did not match. In addition, a manual search of 3 studies were performed and obtained. There were 6 studies that met the inclusion criteria and qualitative studies were carried out which are presented in the following figure.

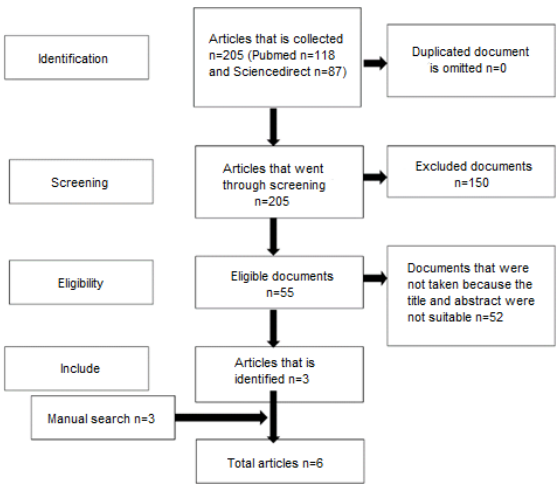

Figure 1. Qualitative Review

RESULTS

Heterogeneity Test

Heterogeneity test was conducted to determine whether fixed effect or random effect will be used. The data were found to be homogeneous and could be accepted if p-value > 0.05. This study had p value = 0.84 (>0.05 then the data is homogeneous) and used fixed effect.

The study conducted by Oncel et al., (2021) found 4 babies infected with Covid-19[15]. Three out of 89 babies born by caesarean section were infected while 1 in 36 babies born through vaginal delivery was infected. Another study conducted by Zeng et al., (2020) found that 3 out of 26 babies born by caesarean section were infected with Covid-19[16], while none of the babies who were born by vaginal delivery infected. A study conducted by Qiancheng et al., (2020) found that out of 22 babies born by vaginal delivery or by caesarean section, none were infected with Covid-19[17]. Farghaly et al., (2020) showed a study included 10 babies who were born by caesarean section and 5 babies were born by vaginal delivery[18]. In this case, 1 in 10 babies born by caesarean section was infected with Covid-19 while no babies born by vaginal delivery were infected with Covid-19[17]. In another study conducted by Ghema et al., (2021), 20 babies were born by caesarean section and 10 babies were born by vaginal delivery[19]. One baby delivered by caesarean section and 1 baby delivered per vaginal were infected. A Spanish study conducted by Martínez-Perez et al., (2020) found that 2 out of 40 babies born by caesarean section were infected with Covid-19 while 41 babies delivered per vaginal did not suffer Covid-19 infection[20].

One study from Qiancheng et al., (2020) did not have an or/ not estimable, and 5 studies (Oncel et al.,2021 ; Farghaly et al.,2020; Zeng et al.,2020; Ghema et al.,2021; Martinez- Perez et al., 2020) had an OR value. The vertical line indicates the line of

no effect (OR=1) and found that 4 studies (Oncel et al,2021; Farghaly et al,2020; Zeng et al.,2020; and Martinez-Perez et al.,2020) were not significant because the horizontal confidence interval line crossed the line of no effect with effect size to the left of the vertical line (OR<1). It means that pregnant women infected with Covid-19 who give birth by caesarean section have a lower probability of the baby not being infected with Covid-19 compared to women who had vaginal delivery. Another study conducted by Ghema et al. (2020) showed that caesarean section delivery to women infected with Covid-19 was a risk factor for babies born negative for Covid-19 (OR>1)[19]. Then, the conclusion of the combined effect with z score =0.82 (p > 0.05) means that the intervention of caesarean section delivery does not have a significant protective factor against negative RT-PCR results in newborn babies.

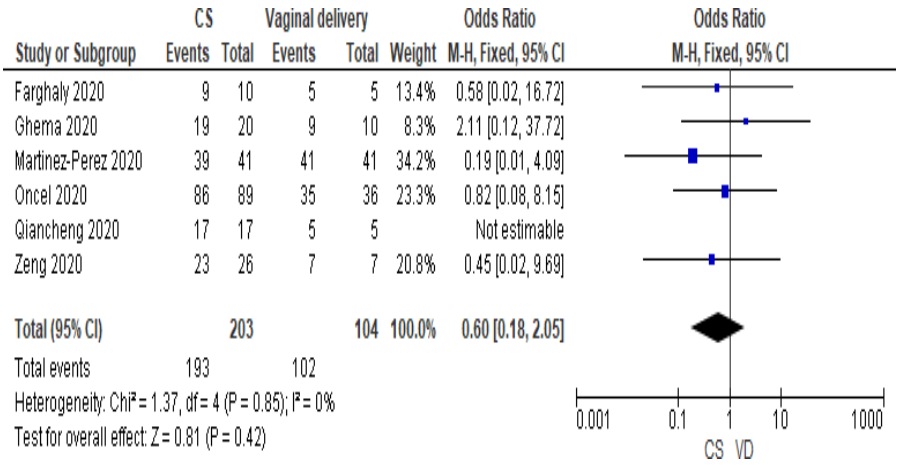

Figure 2. Forest plot

Publication Bias

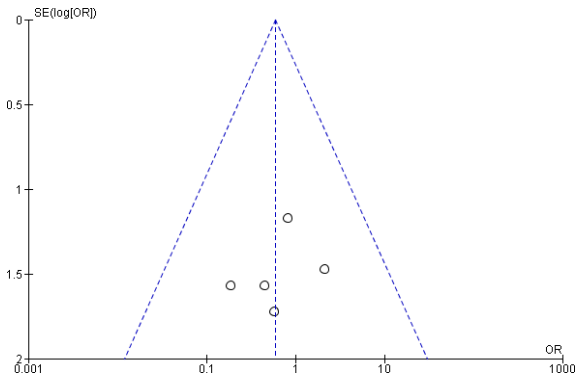

Figure 3. Funnel plot.

Based on the funnel plot above, this study contains a publication bias.

Critical Appraisal

Table 3. Critical appraisal using the cohort studies checklist

	Oncel et al., (2021)[15]		Zeng, et al., (2020)[16]		Martínez-Perez et al., (2020)[20]		Farghaly et al., (2020)[18]		Ghema *et al.*, (2021)[19]		Qiancheng et al., (2020)[17]	
Were the two groups similar and recruited from the same population?	v	V	v	v	v	v	v	v	v	v	v	V
Was the exposure measured in a valid and reliable way?	v	V	v	v	v	v	v	v	v	v	v	V
Were confounding factors identified?	unclear	Unclear	unclear	unclear	unclear	unclear	unclear	unclear	unclear	unclear	unclear	unclear
Were strategies todeal with confound-ding factors stated?	unclear	Unclear	unclear	unclear	unclear	unclear	unclear	unclear	unclear	unclear	unclear	unclear
Were the groups/participants free of the outcome at the start of the study(or at the moment of exposure)?	v	V	v	v	v	v	v	v	v	v	v	V
Were the outcomes measured in a valid and reliable way?	v	V	v	v	v	v	v	v	v	v	v	V

	Oncel et al., (2021)[15]		Zeng, et al., (2020)[16]		Martínez-Perez et al., (2020)[20]		Farghaly et al., (2020)[18]		Ghema *et al.*, (2021)[19]		Qiancheng et al., (2020)[17]	
Was the follow up time reported and sufficient to be long enough for outcomes to occur?	v	V	v	v	v	v	v	v	v	v	v	V
Was follow upcomplete, and if not, were the reasons to lose to follow up described and explored?	v	V	v	v	v	v	v	v	v	v	v	V
Were strategies to address incomplete followup utilized?	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Was appropriate statistical analysis used?	v	V	v	v	v	v	v	v	v	v	v	V

DISCUSSION

Demographic characteristics based on age in pregnant women infected with Covid-19 in the study conducted by Xu et al. (2020) to 28 patients showed the average age of 30 years with a range between 27-32 years[21]. The average age of pregnant women in the study conducted by Farghaly et al. (2020) was 33.4 years[18]. Pregnant women infected with Covid-19 in the study conducted by Martinez-Perez et al[20]. were in the age range of 19-48 years. Pregnant women who gave birth by caesarean section were on average 34.5 years old, while pregnant women who had vaginal delivery were 35 years old on average.

A study conducted by Oncel et al. (2020) found 89 (71.2%) pregnant women gave birth via caesarean section and 36 (28.8%) pregnant women gave birth via vaginal delivery[15]. The study conducted by Zeng et al. found 26 (83.9%) pregnant women who gave birth via caesarean section and 5 (16.1%) pregnant women who gave birth via vaginal delivery. The study by Farghaly et al. (2020) found 10 (67%) pregnant women who gave birth by caesarean section and 5 (33%) through vaginal delivery of a total of 15 pregnant women[18]. A study conducted by Qiancheng et al. (2020)[17] to 28 pregnant women infected with Covid-19, 17 (60.7%) pregnant women were found to give birth

by caesarean section and 5 (17.9%) vaginally, while the remaining 6 continued their pregnancies and had abortions (21.4%).

The study conducted by Farghaly et al. (2020) found 15 pregnant women were positive for Covid-19 from a total of 79 samples (18.98%)[18]. Another study in Morocco conducted by Ghema et al. (2020) found 30 pregnant women were infected with Covid-19, 20 of whom gave birth via caesarean section (66.7%)[19]. In addition, a study conducted by Martinez-Perez et al. (2020) found 37 pregnant women (47%) delivered by caesarean section[20]. Based on the analysis of 4 studies (Oncel et al., 2021; Farghaly et al.,2020; Zeng et al.,2020; and Martinez-Perez et al.,2020) it was found that the way of giving birth to pregnant women infected with Covid-19 through caesarean section has a lower probability of the baby not being infected with Covid- 19 than with women who gave birth by vaginal delivery. Another study conducted by Ghema et al. (2021) showed that giving birth by caesarean section to women infected with Covid-19 was a risk factor for babies who were born negative for Covid-19 (OR> 1)[19]. Meanwhile, one study conducted by Qiancheng et al. (2020) showed results that were not estimable. Delivery by caesarean section has a higher incidence of Covid-19 infection in newborns[17]. From 6 studies, 203 pregnant women who gave birth abdominally had 10 babies born infected with Covid-19 (4.9%). Meanwhile, 104 pregnant women who had vaginal delivery found 2 babies born to be infected with Covid-19 (1.92%). Vaginal transmission in pregnant women infected with Covid-19 is lower. Zheng et al. (2020) argued that the expression of the Covid-19 receptor[16], angiotensin-converting enzyme 2 (ACE2) on fetal and maternal cell surfaces was lower than that of Zika virus. The highest levels of ACE2 expression were in the small intestine, testes, kidneys, heart, thyroid, and adipose tissue and the lowest were in the blood, spleen, bone marrow, brain, blood vessels, and muscles. Another study conducted in Israel found that of 35 women who underwent vaginal swabs, 2 samples (5.7%) were positive for Covid-19 RT-PCR. In China, none of the 10 vaginal swab samples tested positive for Covid-19 RT-PCR[13]. This shows that there is a possibility of colonization of the Covid-19 virus in the vagina which can be a risk factor for newborns infected with Covid-19 due to exposure to vaginal fluids in the birth canal. The conclusion of the combined effect with z score = 0.82 ($p > 0.05$) means that the intervention method of delivery by caesarean section does not have a significant effect on negative RT-PCR results in babies born.

CONCLUSION

The method of giving birth to pregnant women infected with Covid-19 through caesarean section has a lower probability of the baby not being infected with Covid-19 compared to women who have vaginal delivery. The author concludes that there is no association between giving birth by caesarean section in women infected with Covid-19 and the incidence of Covid-19 in newborn. Even so, there are still many bias in this systematic study in which the number of related studies and the sample are still minimal. The rationalization of delivery by caesarean section is based on obstetric indications for both the mother and the fetus. There is a need for large-scale randomized clinical trials or multicenter cohort studies that use the same evaluation parameters to streng

then the quality of subsequent systematic reviews.

ACKNOWLEDGMENT

We thank the Medical Record Department of Dr. Soetomo General Academic Hospital for their assistance in the collection of medical records. We thank the Internal Medicine Department of Dr. Soetomo General Academic Hospital for providing the needed research environment to make this research possible.

CONFLICT OF INTEREST

All Authors have no conflict of interest.

FUNDING

This research was self funded by the authors

AUTHOR CONTRIBUTION

All authors have contributed to all process in this research, including preparation, data gathering and analysis, drafting and approval for publication of this manuscript.

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