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Pregnancy and Covid 19 Infection: Characteristics, Signs, Symptoms, and Impact on Maternal and Neonatal: Systematic Review

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ABSTRACT

The Covid 19 pandemic had a terrible impact on the health system, especially maternal and child health. Covid 19 and MERS infections lead to higher case fatality rates and more severe morbidity during pregnancy. Pregnant women and neonates are a group at risk for the severity of Covid 19 infection. This study aimed to review the characteristics, signs, symptoms, and impact on maternal and neonatal of pregnant women with positive Covid 19. We performed a systematic review to investigate pregnant women infected with Covid 19. Literature research was conducted using several search engines, including Pub Med, Science Direct, and The Lancet, from January 1st, 2021 to March 31th, 2022. The articles were screened based on the inclusion and exclusion criteria based on the PRISMA guidelines. We included 8 studies, the number of pregnant women obtained was 1460 pregnant women with positive COVID 19, 1830 pregnant women with negative COVID-19, and 71 non pregnant women with positive Covid 19. The average age of the mother is around 19-41 years, gestational age is between 25-41 weeks, and the common symptoms are fever, cough, difficulty breathing, or shortness of breath. The most common complications were premature birth and premature rupture of membranes; besides bleeding complications, preeclampsia and fetal distress were reported. The common symptoms are fever and cough, and the impact of maternal are preterm birth and premature rupture of the membranes. The effect of neonatal is low birth weight and premature.

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Kata kunci:

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ABSTRAK

Pandemi Covid 19 memberikan dampak yang sangat buruk bagi sistem kesehatan, khususnya untuk kesehatan ibu dan anak. Infeksi Covid 19 dan MERS menyebabkan tingkat kematian kasus yang lebih tinggi dan tingkat morbiditas yang lebih parah selama kehamilan. Ibu hamil dan neonatus merupakan kelompok yang berisiko untuk terjadinya infeksi Covid-19 yang berat. Penelitian ini bertujuan untuk mengkaji karakteristik, tanda, gejala, dan dampak pada ibu dan bayi baru lahir dari ibu hamil yang positif Covid 19. Penelitian merupakan systematic review yang dilakukan untuk menyelidiki ibu hamil yang terinfeksi Covid 19. Penelitian ini dilakukan dengan melakukan pencarian literatur menggunakan beberapa database pencarian elektronik, antara lain Pub Med, Science Direct, dan The Lancet yang dipublikasi pada satu tahun terakhir yaitu mulai 1 Januari 2021 dan 31 Maret 2022. Artikel yang diperoleh dilakukan screening berdasarkan kriteria inklusi dan eksklusi berdasarkan pedoman PRISMA. Terdapat 8 artikel penelitian yang kami masukkan kedalam penelitian ini yang telah sesuai dengan kriteria inklusi, jumlah ibu hamil yang didapat adalah 1460 ibu hamil positif COVID 19 dan 1830 ibu hamil negatif COVID-19. Rata-rata

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usia ibu sekitar 19-41 tahun, usia kehamilan antara 25-41 minggu, dan gejala yang umum adalah demam, batuk, sulit bernapas, atau sesak napas. Komplikasi yang paling umum adalah kelahiran prematur dan ketuban pecah dini, selain dari komplikasi perdarahan, preeklamsia dan gawat janin juga dilaporkan. Gejala yang umum adalah demam dan batuk, dan dampak dari ibu adalah kelahiran prematur dan ketuban pecah dini. Efek neonatus adalah berat badan lahir rendah dan prematur.

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INTRODUCTION

The Covid 19 pandemic that began in 2019 was first discovered in Wuhan, China, which had a terrible impact on the health system. (Wenling et al. 2020) This virus is very easily transmitted through droplets or airborne.(Harrison, Lin, and Wang 2020) Common symptoms are fever, cough, sore throat, malaise, myalgia, gastrointestinal symptom, anosmia, and ageusia. (Gandhi, Lynch, and del Rio 2020) This virus attack all age groups, including pregnant women, neonates, and newborn. Pregnant women and neonates are a group at risk for the severity of Covid 19 infection. One of the physiological changes that occur during pregnancy is the immune system in pregnant women. Changes in the immune system of pregnant women occur due to the body responding to pregnancy which is considered a foreign object that must be handled. Therefore the body's response produces large amounts of cytokine protein, coupled with the presence of Covid 19 infection. Covid 19 infection in pregnancy can impact the profile of Cytokines in pregnant women, cytokine levels in pregnant women appear to correlate with the severity of Covid 19 disease. (Tanacan et al. 2021)

SARS CoV 2 and MERS infections lead to higher case fatality rates and more severe morbidity during pregnancy. (Schwartz and Graham 2020) Any infection that occurs during pregnancy has a potential risk, including infection with Covid 19, based on recent research saying that 3% of pregnant women infected with SARS-CoV-2 require intensive care. (Zimmermann and Curtis 2020) Very few pregnant women diagnosed with Covid 19 gave birth normally, and more gave birth by cesarean section; this indicates that the complication rate for pregnant women infected with COVID 19 is higher. (Villar et al. 2021).

Several systematic review studies related to COVID-19 infection in pregnancy have been carried out and show that the symptoms commonly experienced by pregnant women are fever and cough. (Do Amaral et al. 2020; Smith et al. 2020) There is much understanding of the impact of covid 19 infection on pregnancy, differences in other populations and risk of vertical transmission from the mother and baby. (Alzamora et al. 2020) In previous systematic reviews, there were no reports of maternal deaths due to covid 19 infection. (Smith et al. 2020) Currently, Covid 19 infection continues to increase in various cities in the world, and this requires the latest research related to the characteristics of pregnant women infected with covid 19 and its impact on mothers and babies to be able to provide an overview and guidelines in handling covid 19 for pregnant women and newborns, therefore, research this article will explain the characteristics, signs, and symptoms as well as the impact of Covid 19 on pregnancy on maternal and neonatal through a systematic review study.

METHOD

This research is systematic review research by taking data from scientific journals published in the last 1 year, starting from January 1, 2021, to March 31, 2022. Literature research was conducted using several search engines, including Pub Med, Science Direct, and The Lancet. Search using keywords "Covid 19" or "SARS CoV-2" and "Pregnancy" or "Maternal" or "Neonatal" and "Effect" or "Outcome" or "Impact". The articles obtained from the three search databases were then checked for duplication using the Mendeley reference manager. Articles that were no longer duplicated were then screened based on the inclusion and exclusion criteria based on the PRISMA guidelines.

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The inclusion criteria of this study are studies that report pregnant women infected with COVID-19 and report characteristics and impacts on maternal and/or neonatal, either analytical or descriptive studies, retrospective or prospective cohort study designs, case series, case-control, observational and cross-sectional, published articles January 2021-March 2022 in Indonesian and English which can be downloaded in full text. The exclusion criteria for this study were non-pregnant COVID-19 infection, articles that did not report characteristics, maternal and/or neonatal impacts, articles using the literature review method, systematic reviews, editorial reviews, correspondence, scoping reviews, integrated reviews, and articles in the form of guidelines and opinions, articles in languages other than Indonesian and English. The flow of the literature search can be seen in Figure 1.

The search results for articles that have gone through the selection are then reviewed using the narrative method. Articles that meet the criteria are summarized, including the researcher's name, year of publication, research methods, and research results covering characteristics, signs, symptoms, and maternal and neonatal impact. Furthermore, the review results are analyzed according to the research objectives, then look for similarities and differences in each research result from each selected article, then discussed and concluded.

RESULTS AND DISCUSSION

The results of this study were obtained from 3 databases PubMed, Science Direct, and The Lancet from January 1, 2021, to January 31, 2022. After a search, 524 articles were found in PubMed, 1090 articles in Science Direct, and 52 in the lancet, with a total of 1666 articles. Of the 1666 articles, duplication was checked using the Mendeley reference manager, and 168 duplicated articles were obtained, 1498 articles were selected for selection, conformity with the inclusion criteria, topics, and research objectives through the selection of article titles, and there were 1360 articles excluded, 138 articles were carried out a feasibility study based on abstracts, and 119 articles were excluded, then 19 articles were then carried out a full-text review, there were 11 articles excluded including 4 articles that did not contain

maternal and neonatal impacts, 1 article with reproductive age population, 2 articles did not report the characteristics of pregnant women and 4 articles in the form of guidelines and opinions. So that 8 articles were found that were suitable and further analysis and discussion were carried out.



Figure 1. Systematic Review Flow Diagram Based on PRISMA 2020

Table 1 Summary of Selected Studies

Author (Year)	Title	Study Design Population		Main Finding		
Nayak, et al. (2021)	Neonatal outcomes of pregnant women with COVID-19 in a developing country setup	Prospective Observational Study	Neonatal was born to SARS - CoV 2 infected mothers (n=165), Pregnant women invected Covid 19 (n =162)	Characteristics of a mother are the most deliveries section Cesaria (63,6%), the average gestational are 37,5 week. Out of 37 symptomatic mothers of Covid 19, 21 had breathing difficulties and required oxygen. There was one maternal death and 5 neonatal death from the mother with positive covid 19 one of them with positive covid 19. The most outcome of neonatal are low birth weight (29,7%) and preterm baby (16,4%)		
A.Almatary,et al.(2021)	Clinical outcomes of maternal and neonate with COVID-19 infection: A multicenter study in Saudi Arabia	Retrospective Cohort	Pregnant women with confirmed Covid-19 infection and their neonates (n: 288)	The characteristic of pregnant women in this study are the median age was 30 years, and the median gestational age was 38 weeks. Two- thirds of deliveries occur by vaginal delivery. Most pregnant women developed Covid 19 symptoms, the most prevalent symptom was cough (31,9). About 9,4% of pregnant women need respiratory support. Most pregnancy outcomes were premature (15,5%) follow by fetal distress (6,5%), preeclampsia (2,0%), and one pregnant woman died.86 neonates required NICU care, three of them had IUGR. There was no neonatal death, however there are 4 fetal death during the pregnancy.		
M. Abedzadeh- Kalahroudi ,et al. (2021)	Clinical and obstetric characteristics of pregnant women with Covid-19: A case series	Case series study	Pregnant women with confirmed Covid-19 infection (n: 26)	The characteristic of pregnant women in this study is the mean age of pregnant women was $30,6 \pm 6,5$ years. The mean gestational age of		

Author (Year)	Author (Year) Title		Population	Main Finding			
	study on 26 patients			the patients at admission and delivery was 31.8 ± 5.2 and 36.3 ± 3.4 weeks. The most type delivery was cesarean section (69,2%). The most common symptom was fever and chills (96,2%). The most mater no fetal outcome was preterm labor (38%), preeclampsia (19,2%). Of 26 newborns, six cases were admitted to the NICU and 2 neonatal death.			
Daclin,et al.(2022	Impact of Covid-19 infection in pregnancy and neonates: A case control study	Case control study	Pregnant women with confirmed Covid-19 infection (n: 86) and Pregnant women with negative Covid-19 (n : 86)	In the Covid 19 group there were 27,5% asymptomatic and 72,5% symptomatic, the most common symptom were fever and cough. The most type of delivery was spontaneous delivery (56,5%). Neonatal outcomes were not statistically different between the two groups. There was no maternal and neonatal death.			
Arinkan,et al.(2021	Perinatal outcomes of pregnant women having SARS-CoV-2 infection	Prospective observational study	Pregnant women with confirmed Covid 19 (n: 46) and healthy pregnant women (n: 70)	There was no significant difference in characteristic gestational age at birth between pregnant women who had Covid 19 infection and those who did not $(37.02 \pm 5.85 \text{ vs } 38.5 \pm 2.33)$. The most common symptom was cough $(41,3\%)$. The most pregnancy outcome was preterm delivery. There were three emergency cesarean sections and two of them died due to Covid 19. One newborn had a positive result for Covid 19.			
C,Ferrugini,et al.(2021)	SARS-CoV-2 infection in pregnant women assisted in a high-risk maternity hospital in Brazil: Clinical aspects and obstetric outcomes	Cros sectional Study	Pregnant women with Covid 19 infection (n: 265)	Most pregnant women were aged 20 to 34 years old. The most frequently reported symptoms were runny nose, cough, loss of smell and taste, headache, and fever. There was also a 35% rate of asymptomatic infections and a 4.6% rate of severe or critical infections. The most outcome of pregnancy was preterm delivery, cesarean section and resuscitation.			
J.Villar, et al.(2021)	Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without Covid-19 Infection	Cohort Study	Pregnant women with Covid 19 infection (n: 706) Pregnant women without Covid 19 infection (n: 1424)	The characteristics of pregnant women in this study are not different from the two groups, however 48,6% of pregnant women with Covid 19 had been overweight early in pregnancy. Women with Covid 19 had a higher rate of hypertension, preeclampsia and infection. Eleven women died due to Covid 19 infection (159/10.000 births). 41% of women with Covid -19 diagnosis were Asymptomatic. The most common symptom was fever and shortness of breath. Women with Covid 19 infection had a higher cesarean delivery rate. They also have higher preterm birth and fetal distress and higher low birth weight rate (RR,1,58:95% CI). The rates of pre labour rupture of membranes were similar in both groups.			
M.S, Asghar, et.al (2022)	COVID-19 infection among pregnant and non-pregnant women: Comparison of biochemical markers and out comes during COVID-19 pandemic, A	Retrospective Cohort Study	Pregnant women with Covid 19 infection (n : 60) and non pregnant women with Covid 19 infection (n: 71)	The characteristic of pregnant women in this study is the mean age lower than non pregnant women. The most common symptom was fever, fatigue, and cough. Mortality rates were 5,0 % in pregnant women versus 15,5% in non pregnant			

Author (Year)	Title		Study Design	Population	Main Finding			
	retrospective cohort study				women. The pregnancy outcome was preeclampsia, premature birth, and stillbirth. Most typesof deliveries were cesarean sections.			

Based on the selection of articles that have been carried out 8 articles were obtained and then analyzed qualitative and narrative. The total number of pregnant women obtained was 3290 pregnant women, 1460 pregnant women with positive COVID 19, 1759 pregnant women with negative COVID-19 as control groups, and 71 non pregnant women with positive Covid 19 as a control groups. The total neonates reported from this study were 605 neonates, 71 neonates were positive for covid 19, and others were not screened. Selected studies came from hospitals in various countries, including India, Saudi Arabia, Iran, Parisian, Turkey, Brazil, Pakistan, and one study involved 18 countries, including Argentina, Brazil, Egypt, France, Ghana, India, Indonesia, Italy, Japan, Mexico, Nigeria, North Macedonia, Pakistan, Russia, Spain, Switzerland, the UK, and the US. The average age of the mother is around 19-41 years, gestational age is between 25-41 weeks, and the symptoms that generally appear are fever, cough, difficulty breathing, or shortness of breath. The most common complications were premature birth and premature rupture of membranes; besides bleeding complications, preeclampsia and fetal distress were reported. The most complications in newborns were premature and low birth weight, and there were reported to be 71 neonates who were positive for covid 19. Most types of delivery were cesarean sections. It was reported that there were 18 cases of maternal death with positive covid 19, and it was reported that there were 5 neonatal deaths, 4 of which were positive for covid. The result of characteristics and maternal signs, symptoms, and impact of COVID-19 on maternal and neonatal can be seen in Table 2

Based on the results of a review of 8 articles, it was found that covid 19 infection in pregnant women can cause morbidity. On the fifth day after the commencement of the condition, the patient had respiratory failure and required mechanical ventilation. (Alzamora et al. 2020) Several studies report maternal deaths due to COVID-19 infection. (Al-Matary et al. 2021; Nayak et al. 2021; Sohaib et al. 2022; Villar et al. 2021) There were 16 cases of maternal death due to covid 19 infections reported in 4 studies; in the group of women with COVID-19 diagnosis, the probability of maternal mortality was 1.6 percent or 22 times greater. COVID-19 in pregnancy can be deadly when comprehensive ICU services are not fully available since these deaths were clustered in institutions from less developed regions.Except for preeclampsia, we discovered that asymptomatic women with COVID-19 diagnosis had similar outcomes to women without COVID-19 diagnosis. (Villar et al. 2021) Most pregnant women testing positive for SARS-CoV-2 were asymptomatic, and none transmitted the virus to their babies. (Zlochiver et al. 2021) Another study also showed that 9 of pregnant women with severe COVID-19 infection, 7 of 9 died, 1 of 9 needed a ventilator and 1 again required a long hospital stay, most of which occurred in the 2nd and 3rd trimesters of pregnancy. (Hantoushzadeh et al. 2020).

In this study, the most common COVID-19 symptoms among pregnant women were cough, fever, and short breath. In a case series study conducted by Shahla Chaichan, et all, the most common symptoms were myalgia and fatigue. However, in most studies, cough, and fever were the most common symptoms. (Chaichian et al. 2021) In this study, the most common type of delivery is by cesarean section. In patients with COVID-19, vaginal delivery is not recommended because there is no strong evidence of vertical transmission; when a dangerously unwell parturient requires an emergency birth, a cesarean section is the best option. (Dashraath P, Wong JLJ, Lim MXK, Lim LM, Li S, Biswas A, Choolani M, Mattar C 2020) A comprehensive review and meta-analysis of generally high-quality studies with suitable comparison groups indicated that pregnant women with SARS-CoV-2 infection had a higher risk of preeclampsia, preterm birth, and stillbirth than those who did not have SARS-CoV-2 disease. (Wei et al. 2021) When compared to those with a mild condition, severe COVID-19 was linked to preeclampsia, premature birth, gestational diabetes, and low birth weight in pregnant women.(Jamieson & Rasmussen, 2021).

Complications in pregnant women who are positive for COVID-19 are PROM, premature birth, and fetal distress. (Ferrugini et al. 2022) In neonates, the most common complications are low birth weight and premature birth. Based on the results of the literature study, it was found that there were more than 15 cases of maternal death due to COVID-19 infection and more than 3 cases of neonatal death from mothers who were positive for COVID-19.

Table 2 Study Characteristics and Maternal Signs, Symptoms, and Impact of COVID-19 on Maternal and Neonatal

	Author							
Variable	Nayak,et al. (2021) (Nayak et al. 2021)	A. Almatary,et al. (2021) (Al- Matary et al. 2021)	M. Abedzadeh- Kalahroudi ,et al. (2021) (Abedzadeh- Kalahroudi et al. 2021)	Daclin,et al. (2022) (Daclin et al. 2022)	Arinkan,et al. (2021) (Arinkan et al. 2021)	C, Ferrugini,et al. (2021) (Ferrugini et al. 2022)	J. Villar, et al. (2021) (Villar et al. 2021)	M S, Asghar, et. al (2022) (Sohaib et al. 2022)
Methods	Prospective Observational Study	Retrospective Descriptive Study	case series study	Case-control retrospective study	prospective observational study	Crossectional study	Multinational cohort study	Retrospective Cohort Study
Pregnant women Positive Covid 19 Negative Covid 19 Non-Pregnant Women Positif Covid 19	162 162 0	288 288 0	26 26 0	172 86 (Case) 86 (Control)	116 46 (Case) 70 (Control)	265 86 179	2130 706 1424	131 60 - 71
Neonatal Location	165 (5 twins) COVID hospital, Odisha state (India)	204 Hospital in Riyadh City in Saudi Arabia	26 University hospital of Kashan Iran	86 Foch Hospital, West Parisian area	116 Umraniye Research and Training Hospital	8 HUCAM maternity hospital Victoria, capital, Brazil	2130 43 institutions in 18 countries (Argentina, Brazil, Egypt, France, Ghana, India, Indonesia, Italy, Japan, Mexico, Nigeria, North Macedonia, Pakistan, Russia, Spain, Switzerland, the UK, and the US).	Liaquat National Hospital, Pakistan
Mean Age Maternal	31 (19-41)	30,0 (35-26)	30,6 (37,1-24,1)	32,1(37,1-27,1)	28s,87(±4,74)	<19 y old : 13(15,1) 20-34 y old : 57 (66,3) ≥35 y old : 16 (18,6)	30,2 (±6,1)	28.11(± 5.24)
Mean Gestational Age	37,5 (25-41)	38 (39-33)	31,8 (37-26,6)	39,29 (2,65)	37,02(5,85)	≤13 weeks : 3 (3,5) 14 w - 27 w : 2 (2,3) 28 w-36 w : 20 (23,3) ≥37 w : 61(70,9)	37,9 (±3,3)	31,46 (±6,13)

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		Author							
	Variable	Nayak,et al. (2021) (Nayak et al. 2021)	A. Almatary,et al. (2021) (Al- Matary et al. 2021)	M. Abedzadeh- Kalahroudi ,et al. (2021) (Abedzadeh- Kalahroudi et al. 2021)	Daclin,et al. (2022) (Daclin et al. 2022)	Arinkan,et al. (2021) (Arinkan et al. 2021)	C, Ferrugini,et al. (2021) (Ferrugini et al. 2022)	J. Villar, et al. (2021) (Villar et al. 2021)	M S, Asghar, et. al (2022) (Sohaib et al. 2022)
1.	Fever	-	44	25	24	-	25	199	37 (61.7%)
2.	Cough	-	92	8	30	41,3%	28	48	41 (68.3%)
3.	Diary	-	8	2	-	2,2%	8	-	19 (31.7%)
4. 5.	Dyspnea/Shortness of breath Sore throat	21	36	8	5	-	16	89	40 (66.7%)
6.	Fatigue	-	33	-	-	-	10	-	-
7.	Myalgia	-	17	-	-	2,2%	-	-	47 (78.3%)
8.	Malaise	-	2	-	-	15.2%	25	-	-
9.	Nausea or vomiting	-	8	-	-	_	-	-	-
10.	Asymptomatic	-	7	-	-	-	-	-	-
11.	Headache	-	41	-	22	-	30	288	-
		-	-	4	0	-	26	-	-
Materna	al Complication / Impact of								
1	Hemorrhage	2	_	_	Δ	_	_	ΔΔ	_
2	PROM	25	16	1	-	_	_	114	_
2.	Preeclampsia	-	4	6	1	_	19	59	5
4.	Fetal distress	27	13	2	-	-	-	87	-
5	Preterm labor	-	31	11	_	6	21	159	4
6.	Miscarriage	-	-	-	-	-	6	-	-
Neonata	al Complication								
1.	Low Birth Weight	49	29	9	0	-	11	145	-
2.	Preterm	27	31	11	-	-	21	159	4
3.	Positive Covid 19	9	0	8	-	1	3	54	-
4.	RDS	8	-	_	-	-	3	-	-
Deliver	ed								
Yes		162	204	26	0.0	46	82	706	57
No		-	84	-	86	-	4	0	3
Mode of	f delivery								
1.	Vaginal	59	131	8	51	-	25	360	15
2.	Section Cesarea	103	73	18	33	-	57	346	42
Materna	al Mortality	1	1	-	-	2	-	11	3
Neonata	al Mortality	5	0	0	-	-	2	-	-
Stillbirt	h/ IUFD	2	4	0	-	-	-	-	2

LIMITATION OF THE STUDY

The limitation of this study is not registered in the International Prospective Register of Systematic Reviews (PROSPERO). Our literature search used three databases only, and our literature search was restricted to publications in English. We did not conduct the meta-analysis, we review and used the narrative method.

CONCLUSIONS AND SUGGESTIONS

Pregnant women generally have the same symptoms as those who are not pregnant. For pregnant women who are positive for Covid 19, fever, cough, and shortness of breath often appear. The most complications that arise from mothers who are positive for COVID-19 are PROM and premature birth. The incidence of maternal deaths that were positive for COVID-19 was recorded in several studies. Strict supervision for pregnant women who are positive for Covid 19 is necessary to avoid seriousness.

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ETHICAL CONSIDERATIONS

We did not seek ethical considerations for this systematic review because the data were publicly available.

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Conflict of Interest Statement

No potential conflicts of interest were reported by the authors. The author is solely responsible for the views expressed in this publication.

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