


Threatened abortion, threatened premature labor, and preterm birth during the first state of emergency for COVID-19 in 2020 in Japan

Sumiyo Okawa^{1,2} , Yoshihiko Hosokawa³, Keiko Nanishi⁴, Masayoshi Zaitzu⁵ and Takahiro Tabuchi²

¹Institute for Global Health Policy Research, Bureau of International Health Cooperation, National Center for Global Health and Medicine, Tokyo, Japan

²Cancer Control Center, Osaka International Cancer Institute, Osaka, Japan

³Department of Obstetrics and Gynecology, Faculty of Medicine, University of Tsukuba, Ibaraki, Japan

⁴Office of International Academic Affairs, Graduate School of Medicine and Faculty of Medicine, The University of Tokyo, Tokyo, Japan

⁵Department of Public Health, School of Medicine, Dokkyo Medical University, Tochigi, Japan

Abstract

Aim: This study examined the maternal experience of threatened abortion, threatened premature labor, or preterm birth before, during, and after the first state of emergency for COVID-19 in 2020 in Japan.

Methods: This was a cross-sectional, internet-based questionnaire survey. We recruited 600 postpartum women and divided them into three groups by date of delivery: before (October 2019–March 2020), during (April–May 2020), and after (June–October 2020) the first state of emergency. The outcome was the presence of at least one of the following complications: threatened abortion, threatened premature labor, and/or preterm birth. The prevalence ratios (PRs) of the outcome were calculated and compared among the three groups using a multivariable Poisson regression model with adjustment for potential confounders.

Results: Of the 553 women eligible for analysis, those who delivered during (PR 0.69, 95% confidence interval [CI] 0.47–0.99) and after (PR 0.62, 95% CI 0.42–0.90) the state of emergency were less likely to have experienced either threatened abortion, threatened premature labor, or preterm birth than those who delivered before the state of emergency. Among the adjustment variables, smoking at the time of survey (PR 1.68, 95% CI 1.01–2.80) and living in the prefectures with a population of >5 million (PR 0.71, 95% CI 0.51–0.97) were associated with the study outcome.

Conclusion: Threatened abortion, threatened premature labor, or preterm birth appeared to decrease during and after the first state of emergency in 2020. The longitudinal effects of coronavirus disease on maternal and newborn health should be monitored continuously.

Key words: COVID-19, maternal health, preterm birth, threatened abortion, threatened premature labor.

Introduction

Pregnant women are vulnerable to natural and human disasters, such as the pandemic of the novel coronavirus disease 2019 (COVID-19). Since the

beginning of the COVID-19 pandemic, the risk of COVID-19 infection to maternal and neonatal health has been a serious concern. Previous studies have reported that infected pregnant women commonly present with fever and cough, and they are more likely to

Received: September 13 2021.

Accepted: February 11 2022.

Correspondence: Sumiyo Okawa, Institute for Global Health Policy Research, Bureau of International Health Cooperation, National Center for Global Health and Medicine, Postal address: 1-21-1, Toyama, Shinjuku-ku, Tokyo, 162-8655, Japan.

Email: sokawa@it.ncgm.go.jp

require intensive care or invasive ventilation than infected nonpregnant women.¹ Furthermore, infected pregnant women were more likely to experience preterm birth, while their newborns were more likely to need neonatal care unit admission than uninfected pregnant women and their newborns.¹ Among 256 newborns born to mothers infected with COVID-19, four (1.6%) were tested positive for the virus.² These data show that the COVID-19 outbreak is a threat to both pregnant women and their newborns.

During the COVID-19 pandemic, pregnant women encountered socio-environmental changes that they had never experienced before, such as movement restrictions and limited access to maternity care services. Pregnant women were restrained from antenatal care visits or institutional delivery in India and Nepal,^{3,4} received less medical counseling and social support in Belgium,⁵ and had limited opportunities to receive support for breastfeeding and childcare in the United Kingdom.⁶ In this unusual situation, more pregnant and postpartum women experienced anxiety and depression.^{7,8} Furthermore, studies have reported that the incidence of gestational diabetes and hypertensive disorders of pregnancy increased in Israel,⁹ and control of gestational diabetes deteriorated in France.¹⁰ Meanwhile, some positive changes were observed, such as the number of premature births decreased in Denmark and the Netherlands^{11,12} and the number of newborns born with very low birth weight decreased in Ireland.¹³ Regarding other natural disasters, a small increase in the incidence of preterm birth was observed in the area affected by ice storm,¹⁴ whereas no change in its incidence was reported in areas affected by a major earthquake¹⁵ or flood.¹⁶ The influence of COVID-19 on pregnant women's health and birth outcomes may not necessarily be similar to that of other natural disasters.

Preterm birth occurs through multiple mechanisms, including intrauterine infection/inflammation, uterine ischemia, uterine overdistension, allergic phenomena, cervical insufficiency, or hormonal disorders.¹⁷ Working long hours or engaging in stressful physical labor are known risk factors for preterm birth.^{18–20} The potential mechanism for the decrease in preterm birth during the COVID-19 lockdown is considered to be the reduction of infection-related inflammation or physical stress due to hygiene practices and stay-home obligations.^{11,12}

In Japan, the national government first declared the state of emergency to seven prefectures on April 7, 2020, and officially ended the restriction on May 25, 2020.²¹ The number of confirmed cases of and

deaths due to COVID-19 in the country as of April 7, 2020, were 3906 and 80, respectively, which were fewer than that of the majority of European and North American countries.²² Although the government did not apply a lockdown measure, it strongly requested that individuals practice basic hygiene, self-restrict going out, and work from home. As for pregnant women, the government requested employers to assess COVID-19-related anxiety and stress in pregnant women and make necessary arrangements to improve work conditions or environments for these women.²³ The Japan Society of Obstetrics and Gynecology and Japan Association of Obstetricians and Gynecologist announced several suggestions to prevent further transmission of COVID-19, including pregnant women may need to extend the interval between antenatal check-ups and be restrained from returning to their hometown for delivery²⁴ and staying at their parents' home to receive their support during pregnancy and the postpartum period, although these are common practices in Japan. From January to June 2020, an estimated 0.03% of pregnant women were confirmed to have COVID-19 in 1418 facilities across the country.²⁵ Furthermore, a study reported that the number of neonatal intensive care unit admissions, neonatal resuscitation, and preterm birth decreased during the COVID-19 outbreak, based on the administrative data of 186 hospitals.²⁶ To further assess this evidence, we examined the incidence of threatened abortion, threatened premature labor, and preterm birth before, during, and after the first state of emergency for COVID-19 in 2020 in Japan, based on maternal reports.

Methods

Study design, setting, and data source

This is a cross-sectional, internet-based questionnaire survey and part of the "Japan COVID-19 and Society Internet Survey (JACSIS) study." The JACSIS study consisted of three surveys with the following targets: general population, pregnant and postpartum women, and adults from single-parent households. The study samples for each survey were retrieved from the pooled panels of an internet research agency (Rakuten Insight, Inc.), which had approximately 2.2 million panelists in 2019.²⁷ Of the three surveys, we used the data of the pregnant and postpartum women survey. Of the 21 896 women who had given birth later than October 2019 or were expected to give birth

by March 2021, 4373 were selected using simple random sampling and received an invitation e-mail to participate in the survey. Women who had a miscarriage or preterm birth were excluded at recruitment. Data collection began on October 15, 2020, and ended on October 25, 2020, when the sample size reached the target of 1000 women (i.e., 400 pregnant women and 600 postpartum women).

The survey questionnaire consisted of demographic and socioeconomic characteristics of the women, the profile of their latest pregnancy, including complications experienced by women during pregnancy, and the health status of newborns at birth. Women responded to the questionnaire, which was based on the information documented in the Maternal and Child Health Handbook that all pregnant women were provided by the local administration, and their health information was recorded by healthcare professionals at every check-up. The question items on maternal complications during pregnancy included threatened abortion, threatened premature labor, preterm birth (i.e., birth before the 37th week of gestation), hypertensive disorders of pregnancy, gestational diabetes, preeclampsia, placenta previa, placental abruption, worsened pre-existing illnesses, or other medical conditions requiring hospitalization. The two question items on neonatal health status within the first 7 days after birth included low birth weight (i.e., <2500 g) and neonatal intensive care unit admission. Other information on the profile of the latest pregnancy was parity, whether the latest pregnancy was planned, whether it was conceived by fertility treatment, frequency of antenatal care visits, and whether the delivery was assisted by cesarean section. Information regarding the history of COVID-19 was not collected.

Study sample

The inclusion criteria of the study sample were women who had live births between October 2019 and October 2020. Of the 600 postpartum women who participated in this study, we excluded seven women who had multiple births and 40 who gave unnatural or inconsistent responses according to our pre-determined definition. One woman who had a cesarean section due to suspected COVID-19 was included in the analysis. This resulted in a final sample of 553 postpartum women for the analysis.

Exposure variables

The included women were categorized into three groups by date of delivery, with a focus on the period in which the first state of emergency was adopted

between April and May 2020. Thus, we categorized women by having delivered between October 2019 and March 2020 (before the state of emergency), between April and May 2020 (during the state of emergency), or between June and October 2020 (after the state of emergency). The sample sizes for each group were 185, 187, and 181, respectively (Table 1).

Outcome variable

The outcome variable was whether a woman experienced threatened abortion, threatened premature labor, and/or preterm birth during the last pregnancy or delivery.

Adjustment variables

We adjusted for the women's characteristics: age (categorized as groups by years: 21–29, 30–34, 35–39, or 40–43), parity (primipara or multipara), planned pregnancy (yes or no), conception by fertility treatment (yes or no), the frequency of antenatal care visit (reduced or not reduced), having had at least one of the seven complications during pregnancy (i.e., hypertensive disorders of pregnancy, gestational diabetes, preeclampsia, placenta previa, placental abruption, progress of pre-existing illnesses, or other medical condition requiring hospitalization) (yes or no), annual household income in 2019 (<5 million, 5–7.9 million, or ≥8 million by Japanese yen), work type (office work, interpersonal work, physical work, or never worked after January 2019), partner support based on whether a woman does not receive at least one of the three supports (i.e., support given by partner when a woman is in need, emotional acceptance by partner, or sharing housework and childcare with partner) (poor or not poor), smoking status at the time of survey (smoking every day or sometimes, never or previously smoked), and prefecture where a woman resides (prefectures with populations greater or less than 5 million individuals²⁸).

Statistical analysis

We compared the sociodemographic characteristics and complications experienced by women during pregnancy and the health status of their newborns. We then focused on threatened abortion, threatened premature labor, or preterm birth and compared the incidence of having at least one of the three complications among women who delivered before, during, and after the state of emergency using a multivariable Poisson regression model with adjustment for the abovementioned confounders. Using the same regression model, the incidence of each complication (i.e., threatened abortion,

TABLE 1 Basic characteristics of the participating women

	Dates of delivery				p-value
	Oct. 2019–Mar. 2020	Apr. 2020–May 2020	Jun. 2020–Oct. 2020	Total	
	n (%)	n (%)	n (%)	n (%)	
Total	185 (33.5)	187 (33.8)	181 (32.7)	553 (100.0)	
Socio-demographic characteristics					
Age					0.30
21–29	52 (28.1)	43 (23.0)	43 (23.8)	138 (25.0)	
30–34	82 (44.3)	95 (50.8)	79 (43.7)	256 (46.3)	
35–39	40 (21.6)	45 (24.1)	48 (26.5)	133 (24.1)	
40–43	11 (6.0)	4 (2.1)	11 (6.1)	26 (4.7)	
Parity					0.07
Primipara	94 (50.8)	107 (57.2)	82 (45.3)	283 (51.2)	
Multipara	91 (49.2)	80 (42.8)	99 (54.7)	270 (48.8)	
Planned pregnancy					0.63
Yes	155 (83.8)	159 (85.0)	158 (87.3)	472 (85.4)	
No	30 (16.2)	28 (15.0)	23 (12.7)	81 (14.7)	
Conception by fertility treatment					0.17
Yes	25 (13.5)	32 (17.1)	38 (21.0)	95 (17.2)	
No	160 (86.5)	155 (82.9)	143 (79.0)	458 (82.8)	
Antenatal care visit					0.11
Reduced	4 (2.2)	12 (6.4)	11 (6.1)	27 (4.9)	
Did not reduce	181 (97.8)	175 (93.6)	170 (93.9)	526 (95.1)	
Mode of delivery					0.71
Vaginal delivery	143 (77.3)	151 (80.8)	146 (80.7)	440 (79.6)	
Cesarean section due to suspected COVID-19	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.2)	
Emergency cesarean section	20 (10.8)	16 (8.6)	13 (7.2)	49 (8.9)	
Planned cesarean section	21 (11.4)	20 (10.7)	22 (12.2)	63 (11.4)	
Marital status					0.79
Married	184 (99.5)	185 (98.9)	180 (99.5)	549 (99.3)	
Not married	1 (0.5)	2 (1.1)	1 (0.6)	4 (0.7)	
Household income (million yen)					0.25
<5 million	67 (36.2)	54 (28.9)	49 (27.1)	170 (30.7)	
5–7.9 million	59 (31.9)	73 (39.0)	62 (34.3)	194 (35.1)	
≥8 million	44 (23.8)	38 (20.3)	45 (24.9)	127 (23.0)	
Declined to answer or do not know	15 (8.1)	22 (11.8)	25 (13.8)	62 (11.2)	
Work type					0.02*
Office	54 (29.2)	53 (28.3)	58 (32.0)	165 (29.8)	
Interpersonal	51 (27.6)	52 (27.8)	35 (19.3)	138 (25.0)	
Physical	33 (17.8)	40 (21.4)	22 (12.2)	95 (17.2)	
Never worked after January 2019	47 (25.4)	42 (22.5)	66 (36.5)	155 (28.0)	
Partner support					0.76
Poor support	11 (6.0)	8 (4.3)	9 (5.0)	28 (5.1)	
Not poor support	174 (94.1)	179 (95.7)	172 (95.0)	525 (94.9)	
Smoking at the time of survey					0.76
Smoking every day or sometimes	10 (5.4)	8 (4.3)	7 (3.9)	25 (4.5)	
Never or previously smoked	175 (94.6)	179 (95.7)	174 (96.1)	528 (95.5)	
Prefecture of residence					0.43
Prefectures with population > 5 million	109 (58.9)	121 (64.7)	107 (59.1)	337 (60.9)	
Prefectures with population < 5 million	76 (41.1)	66 (35.3)	74 (40.9)	216 (39.1)	

*p-Value < 0.05.

threatened premature labor, and preterm birth) was compared based on the delivery dates and reported in Supporting Information. Furthermore, we calculated the percentage of preterm birth among those who had threatened abortion or threatened premature labor and reported it in Supporting Information. A *p*-value of <0.05 was considered statistically significant. All analyses were performed using Stata version 15.1 (StataCorp LLC; College Station, TX, USA).

Ethical considerations

This study was approved by the Institutional Review Board of the Osaka International Cancer Institute on June 19, 2020 (approval number: 20084). This internet survey was conducted anonymously, and informed consent was obtained from each woman at the beginning of the survey.

Results

Table 1 shows the distribution of the basic characteristics of the women in the three groups. Of the 553 women, 46.3% were aged 30–34 years and 51.2% were primiparous. More than 85% had planned for this pregnancy, and 17.2% conceived with the assistance of fertility

treatment. Only 2.2% of women who delivered before the state of emergency reduced the number of antenatal care visits, whereas more than 6% of those who delivered during or after the state of emergency did so (*p* = 0.11). Approximately 5% smoked combustible or heated tobacco every day or sometimes at the time of the survey. Sixty percent were living in prefectures with a population of >5 million. Of the basic characteristics, the distribution of work type was significantly different among the three groups (*p* = 0.02).

Table 2 shows complications and health problems experienced by women or their newborns. The percentage of women who had either threatened abortion, threatened premature labor, or preterm birth was 28.7%, 19.8%, and 18.2% before, during, and after the first state of emergency, respectively (*p* = 0.04). The percentage of women who had at least one complication other than the abovementioned complications was 17.3%, 17.1%, and 17.7% before, during, and after the state of emergency, respectively (*p* = 0.99). The percentage of neonates whose birth weight was <2500 g was approximately 9% across the three periods (*p* = 0.95).

Table 3 shows the associations of delivery dates and adjustment variables with having either threatened abortion, threatened premature labor, or preterm birth. Women who delivered during (adjusted

TABLE 2 Maternal complications during pregnancy and delivery and their newborns' health

	Dates of delivery				<i>p</i> -value
	Oct. 2019–Mar. 2020	Apr. 2020–May 2020	Jun. 2020–Oct. 2020	Total	
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	
Experienced threatened abortion, threatened premature labor, or preterm birth	53 (28.7)	37 (19.8)	33 (18.2)	123 (22.2)	0.04*
Threatened abortion	19 (10.3)	15 (8.0)	9 (5.0)	43 (7.8)	0.17
Threatened premature labor	42 (22.7)	28 (15.0)	27 (14.9)	97 (17.5)	0.08
Preterm birth within 37 gestational weeks	11 (6.0)	5 (2.7)	6 (3.3)	22 (4.0)	0.23
At least one of the following seven maternal complications	32 (17.3)	32 (17.1)	32 (17.7)	96 (17.4)	0.99
Hypertensive disorders of pregnancy	12 (6.5)	10 (5.4)	12 (6.6)	34 (6.2)	0.85
Gestational diabetes	6 (3.2)	12 (6.4)	9 (5.0)	27 (4.9)	0.36
Preeclampsia	1 (0.5)	1 (0.5)	3 (1.7)	5 (0.9)	0.43
Placenta previa	4 (2.2)	7 (3.7)	6 (3.3)	17 (3.1)	0.66
Placental abruption	2 (1.1)	1 (0.5)	0 (0.0)	3 (0.5)	0.37
Worsened preexisting illnesses	6 (3.2)	8 (4.3)	3 (1.7)	17 (3.1)	0.34
Other medical conditions requiring hospitalization	7 (3.8)	7 (3.7)	7 (3.9)	21 (3.8)	1.00
Birth weight < 2500 g	18 (9.7)	18 (9.6)	16 (8.8)	52 (9.4)	0.95
Admitted in neonatal intensive care unit	13 (7.0)	10 (5.4)	14 (7.7)	37 (6.7)	0.64

**p*-Value <0.05.

TABLE 3 Associations of delivery dates and adjustment variables with having either threatened abortion, threatened premature labor, or preterm birth

	Experienced outcome		<i>p</i> -value	Adjusted PR	(95% CI)
	Yes	No			
	<i>n</i> (%)	<i>n</i> (%)			
Total	123 (22.2)	430 (77.8)			
Date of delivery			0.04		
September 2019–March 2020	53 (28.7)	132 (71.4)		1.00	
April 2020–May 2020	37 (19.8)	150 (80.2)		0.69	(0.47–0.99)*
June 2020–October 2020	33 (18.2)	148 (81.8)		0.62	(0.42–0.90)*
Age			0.06		
21–29	29 (21.0)	109 (79.0)		1.00	
30–34	69 (27.0)	187 (73.1)		1.30	(0.88–1.92)
35–39	20 (15.0)	113 (85.0)		0.70	(0.41–1.19)
40–43	5 (19.2)	21 (80.8)		0.79	(0.33–1.86)
Parity			0.16		
Primipara	56 (19.8)	227 (80.2)		1.00	
Multipara	67 (24.8)	203 (75.2)		1.32	(0.93–1.87)
Planned pregnancy			0.57		
Yes	103 (21.8)	369 (78.2)		1.00	
No	20 (24.7)	61 (75.3)		1.22	(0.78–1.89)
Conception by fertility treatment			0.61		
Yes	23 (24.2)	72 (75.8)		1.00	
No	100 (21.8)	358 (78.2)		0.79	(0.52–1.20)
Antenatal care visit			0.64		
Reduced	7 (25.9)	20 (74.1)		1.00	
Not reduced	116 (22.1)	410 (78.0)		1.01	(0.55–1.88)
Complications ^a			0.21		
Yes	26 (27.1)	70 (72.9)		1.38	(0.95–2.00)
No	97 (21.2)	360 (78.8)		1.00	
Household income (yen last year)			0.75		
<5 million	38 (22.4)	132 (77.7)		1.00	
5–7.9 million	42 (21.7)	152 (78.4)		1.04	(0.70–1.52)
≥8 million	26 (20.5)	101 (79.5)		1.05	(0.67–1.64)
Declined to answer or do not know	17 (27.4)	45 (72.6)		1.24	(0.77–2.00)
Work type			0.68		
Office	37 (22.4)	128 (77.6)		1.00	
Interpersonal	26 (18.8)	112 (81.2)		0.73	(0.47–1.14)
Physical	24 (25.3)	71 (74.7)		1.08	(0.69–1.69)
Never worked after January 2019	36 (23.2)	119 (76.8)		0.88	(0.57–1.36)
Partner support			0.30		
Poor support	4 (14.3)	24 (85.7)		0.65	(0.27–1.56)
Not poor support	119 (22.7)	406 (77.3)		1.00	
Smoking status			0.03		
Smoking every day or sometimes	10 (40.0)	15 (60.0)		1.68	(1.01–2.80)*
Never or previously smoked	113 (21.4)	415 (78.6)		1.00	
Place of residence			0.04		
Prefectures with population > 5 million	65 (19.3)	272 (80.7)		0.71	(0.51–0.97)*
Prefectures with population < 5 million	58 (26.9)	158 (73.2)		1.00	

Abbreviations: CI, confidence interval; PR, prevalence ratio; ^aComplications: having had at least one of the following seven complications during pregnancy (i.e., hypertensive disorders of pregnancy, gestational diabetes, preeclampsia, placenta previa, placental abruption, progress of pre-existing illnesses, or other medical conditions requiring hospitalization) and **p*-Value < 0.05.

prevalence ratio [aPR] 0.69, 95% CI 0.47–0.99) and after (aPR 0.62, 95% CI 0.42–0.90) the first state of emergency were less likely to experience these problems than those who delivered before the state of

emergency. Regarding adjustment variables, those who smoked every day or sometimes were more likely to have experienced one of these problems than those who had never or previously smoked (aPR 1.68,

95% CI 1.01–2.80). Those who were living in prefectures with a population of >5 million were less likely to have experienced one of these problems than those living in prefectures with a population of <5 million (aPR 0.71, 95% CI 0.51–0.97).

Table S1 reveals the associations of the delivery date with threatened abortion, threatened premature labor, and preterm birth, with adjustment for potential confounders (Supporting Information). The odds of threatened abortion, threatened premature labor, and preterm birth tended to be lower in those who delivered during and after the state of emergency than those who delivered before the first state of emergency, although they were not necessarily significant.

Table S2 presents the percentage of preterm birth among women who had threatened abortion or threatened premature labor during pregnancy. Among 114 eligible women, the percentage of those who had preterm birth was 14.3%, 8.6%, and 10.0% among women who delivered before, during, and after the first state of emergency, respectively, with no significant difference.

Discussion

This study assessed preterm delivery and its related complications during pregnancy that might have been affected by lifestyle changes during the first state of emergency for COVID-19. We found that women who delivered between April and May 2020 (during the state of emergency) were less likely to have experienced threatened abortion, threatened premature labor, or preterm delivery than those who delivered between October 2019 and March 2020 (before the state of emergency). This finding was similar to that of a previous study that reported a decline in preterm birth in Japan between the calendar weeks 10 and 17 (nearly March and April) of 2020, compared with that between the calendar weeks of 2 and 9 (January and February) of 2020.²⁶ Furthermore, our study found that the percentage of women who experienced threatened abortion, threatened premature labor, or preterm birth was continuously low in women who delivered between June and October of 2020 after the state of emergency.

Although we should carefully interpret this result because this study had a small sample size and measured self-reported incidence of perinatal complications, we considered the results reasonable for the following reasons. First, threatened abortion and

threatened premature labor are relatively soft endpoints, which may lead to different diagnoses and indications for hospitalization, depending on the change in the situation of the COVID-19 pandemic and its effect on the functions of hospital systems. However, the incidence of threatened abortion, threatened premature labor, and preterm birth per delivery date showed a nearly identical tendency (Table S1, Supporting Information). Second, our findings may also be supported by the evidence of nationwide reduction of preterm births during the lockdown in Denmark, the Netherlands, and Japan.^{11,12,26} An underlying mechanism discussed in these studies was that lockdown or movement restriction measures led to a decrease in infection load and physical stress, which are common risk factors for preterm birth, resulting in the reduction of preterm births in these countries.^{11,12} In this study, we observed the lowest incidence of threatened abortion, threatened premature labor, or preterm birth in women who delivered after the state of emergency. Although we have insufficient data to explain the reasons for the further decline, this could be explained by the fact that these women might have a longer period of decreased active movement during and after the state of emergency and maternity leave than those who delivered before or during the state of emergency.

Although our finding implies that the decrease in excessive physical activity or stress due to movement restrictions may be associated with the reduced risk of threatened abortion, threatened premature labor, and preterm birth during the first state of emergency, the benefits of physical exercise and the risk of sedentary activity should be noted. Systematic review and meta-analysis studies reported that physical activity (e.g., leisure-time activity and walking) was inversely associated with high gestational weight gain,²⁹ gestational diabetes,³⁰ preeclampsia,³¹ or preterm birth.³² Combining the evidence with our findings, physical activity that aims at maintaining healthy pregnancy should be assured even during the pandemic which requires movement restrictions. A detailed measurement of the frequency and intensity of physical activity and the association with preterm birth and other pregnancy-related complications would be worth investigating in a future study.

Women living in nine prefectures with a population of >5 million were less likely to have experienced threatened abortion, threatened premature labor, or preterm birth. Of these prefectures, eight had the highest population density in the country,³³ and

seven were the first prefectures that were designated as the state of emergency in April 2020²¹ owing to the higher incidence of COVID-19. Although we cannot explain this result with a causal relationship owing to the lack of data on self-restraint preventive behavior or accessibility to maternity care services, an interpretation could be that women living in urban areas might have perceived themselves to be at a high risk of COVID-19 and practiced self-restraint measures with high compliance and for long periods, or these women living in urban areas have good access to maternity care services, allowing them to respond to complications easily as the need arises. These situations may be related to the association between living in an urban prefecture and the study outcome.

Among potential confounders, women who used combustible or heated tobacco at the time of the survey (i.e., in the postpartum period) were more likely to have experienced threatened abortion, threatened premature labor, or preterm birth. We should carefully interpret the result because we cannot explain the causal relationship due to the lack of data on smoking status during pregnancy. However, a potential explanation is that some women who were smoking in the postpartum period might have also smoked before or during pregnancy, which might have affected the study outcome as previous studies reported smoking increased the risk of preterm birth.^{34,35} A further study that examines smoking status during pregnancy and the postpartum period will be worth conducting.

This study has several limitations. First, the study participants may not represent the general population because we used pooled panelists from an internet survey agency and excluded women who had miscarriages or stillbirths from study participation. Moreover, women who had a difficult experience with the latest pregnancy might have declined to participate in the study, which would bias our results. Second, the measurement of the study outcome was potentially biased due to the following reasons. Self-reported data on maternal and neonatal health status might have compromised data accuracy. To maximize accuracy, we requested women to cross-check the health records in the Maternal and Child Health Handbook as a reference. In addition, varying criteria of diagnosis followed by physicians might affect the measurement of the study outcome. Moreover, the number of diagnosed cases might have decreased due to movement restrictions during the state of emergency, including maternal care service visits. The lack of data on the causes of preterm birth might have biased the

interpretation of the study results because some women had to terminate pregnancy during the preterm period due to medical reasons. Third, dividing women by the expected date of delivery might have provided a clearer association between the state of emergency and the study outcome. However, we categorized women by the actual date of delivery because we sampled them in the same manner. Fourth, whether the change in the incidence of the study outcome occurred immediately after the declaration of the state of emergency cannot be demonstrated in this study because we did not analyze the data using a regression discontinuity design or compare the incidence of the study outcome per month due to the small sample size. Finally, we could not adjust for some critical factors in the regression model, such as workload, mental status, hygiene practice, or infection episodes of the women during pregnancy and the quality of maternity care and treatment that could be affected by the COVID-19 pandemic because we did not collect data on these items.

Despite these limitations, this study revealed that the incidence of threatened abortion, threatened premature labor, or preterm birth appeared to have decreased during and after the first state of emergency for COVID-19 in 2020 in Japan. Since the findings are still elusive, we have been conducting a larger-scale follow-up survey since July 2021, which will allow us to evaluate perinatal morbidity using detailed clinical information.

Acknowledgments

This study was funded by the Japan Society for the Promotion of Science (JSPS) KAKENHI Grants (grant numbers: 18H03062; 19K19452; 21H04856), and Health Labour Sciences Research Grant (grant numbers: 19FA1005; 19FA1012). The findings and conclusions of this manuscript are the sole responsibility of the authors and do not represent the official views of the research funders. The authors thank Prof. Hiroyasu Iso at the Institute for Global Health Policy Research, Bureau of International Health Cooperation, National Center for Global Health and Medicine for his technical support.

Author Contribution

Sumiyo Okawa, Yoshihiko Hosokawa, and Takahiro Tabuchi designed the study. Sumiyo Okawa

performed statistical analysis. Sumiyo Okawa and Yoshihiko Hosokawa interpreted the results. Sumiyo Okawa drafted the manuscript. All authors reviewed, critically evaluated the draft, and approved the final draft. Takahiro Tabuchi supervised the study.

Conflicts of Interest

The authors have no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

- Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ*. 2020;**370**:m3320.
- Elshafeey F, Magdi R, Hindi N, Elshebiny M, Farrag N, Mahdy S, et al. A systematic scoping review of COVID-19 during pregnancy and childbirth. *Int J Gynaecol Obstet*. 2020;**150**(1):47–52.
- Ashish KC, Gurung R, Kinney MV, Sunny AK, Md M, Basnet O, et al. Effect of the COVID-19 pandemic response on intrapartum care, stillbirth, and neonatal mortality outcomes in Nepal: a prospective observational study. *Lancet Glob Health*. 2020;**8**(10):e1273–e81.
- Goyal M, Singh P, Singh K, Shekhar S, Agrawal N, Misra S. The effect of the COVID-19 pandemic on maternal health due to delay in seeking health care: experience from a tertiary center. *Int J Gynaecol Obstet*. 2021;**152**:231–235.
- Ceulemans M, Verbakel JY, Van Calsteren K, Eerdekens A, Allegaert K, Foulon V. SARS-CoV-2 infections and impact of the COVID-19 pandemic in pregnancy and breastfeeding: results from an observational study in primary Care in Belgium. *Int J Environ Res Public Health*. 2020;**17**(18):6766.
- Vazquez-Vazquez A, Dib S, Rougeaux E, Wells JC, Fewtrell MS. The impact of the Covid-19 lockdown on the experiences and feeding practices of new mothers in the UK: preliminary data from the COVID-19 new mum study. *Appetite*. 2021;**156**:104985.
- Yan H, Ding Y, Guo W. Mental health of pregnant and postpartum women during the coronavirus disease 2019 pandemic: a systematic review and meta-analysis. *Front Psychol*. 2020;**11**:617001.
- Hessami K, Romanelli C, Chiurazzi M, Cozzolino M. COVID-19 pandemic and maternal mental health: a systematic review and meta-analysis. *J Matern Fetal Neonatal Med*. 2020;1–8.
- Justman N, Shahak G, Gutzeit O, Zvi DB, Ginsberg Y, Solt I, et al. Lockdown with a Price: the impact of the COVID-19 pandemic on prenatal care and perinatal outcomes in a tertiary care center. *Isr Med Assoc J*. 2020;**9**(22):467–71.
- Ghesquière L, Garabedian C, Drumez E, Lemaître M, Cazaubiel M, Bengler C, et al. Effects of COVID-19 pandemic lockdown on gestational diabetes mellitus: a retrospective study. *Diabetes Metab*. 2021;**47**(2):101201.
- Hedermann G, Hedley PL, Bækvad-Hansen M, Hjalgrim H, Rostgaard K, Poorisrisak P, et al. Danish premature birth rates during the COVID-19 lockdown. *Arch Dis Child Fetal Neonatal Ed*. 2021;**106**(1):93–5.
- Been JV, Burgos Ochoa L, Bertens LCM, Schoenmakers S, Steegers EAP, Reiss IKM. Impact of COVID-19 mitigation measures on the incidence of preterm birth: a national quasi-experimental study. *Lancet Public Health*. 2020;**5**(11):e604–e11.
- Philip RK, Purtill H, Reidy E, Daly M, Imcha M, McGrath D, et al. Unprecedented reduction in births of very low birthweight (VLBW) and extremely low birthweight (ELBW) infants during the COVID-19 lockdown in Ireland: a ‘natural experiment’ allowing analysis of data from the prior two decades. *BMJ Glob Health*. 2020;**5**(9):e003075.
- Auger N, Kuehne E, Goneau M, Daniel M. Preterm birth during an extreme weather event in Québec, Canada: a “natural experiment”. *Matern Child Health J*. 2011;**15**(7):1088–96.
- Hawkins G, Gullam J, Belluscio L. The effect of a major earthquake experienced during the first trimester of pregnancy on the risk of preterm birth. *Aust N Z J Obstet Gynaecol*. 2019;**59**(1):82–8.
- Hetherington E, Adhikari K, Tomfohr-Madsen L, Patten S, Metcalfe A. Birth outcomes, pregnancy complications, and postpartum mental health after the 2013 Calgary flood: a difference in difference analysis. *PLoS One*. 2021;**16**(2):e0246670.
- Romero R, Espinoza J, Kusanovic JP, Gotsch F, Hassan S, Erez O, et al. The preterm parturition syndrome. *BJOG*. 2006;**113**(Suppl 3):17–42.
- Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet*. 2008;**371**(9606):75–84.
- Green J, Petty J, Whiting L, Fowler C. Exploring modifiable risk-factors for premature birth in the context of COVID-19 mitigation measures: a discussion paper. *J Neonatal Nurs*. 2020;**27**(3):172–9.
- Takahata H, Siraishi M. Association of occupational stress during pregnancy with premature birth and small for gestational age: a systematic review of observational studies. *J Jpn Acad Midwif*. 2020;**34**(1):25–37.
- Cabinet Secretariat Government of Japan Report on the implementation of the declaration of the state of emergency for the novel corona virus infectious disease. 2020: [cited 26 Aug 2021]. Available from: https://corona.go.jp/news/pdf/kinkyujitaisengen_houkoku0604.pdf.
- The World Health Organization Coronavirus disease (COVID-19) Situation Report —78. 2020: [cited 26 Aug 2021]. Available from: <https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200407-sitrep-78-covid-19.pdf>.
- The Ministry of Health Labour and Welfare To working pregnant women and employers: maternal health management measures for the novel corona virus infectious disease.

- 2021: [cited 2021 Aug 25]. Available from: <https://www.mhlw.go.jp/content/11900000/000628248.pdf>.
24. Japan Society of Obstetrics and Gynecology Notification to pregnant women. 2020: [cited 2021 Aug 25]. Available from: http://www.jsog.or.jp/uploads/files/news/20200407_COVID19.pdf.
 25. Arakaki T, Hasegawa J, Sekizawa A, Ikeda T, Ishiwata I, Kinoshita K. Clinical characteristics of pregnant women with COVID-19 in Japan: a nationwide questionnaire survey. *BMC Pregnancy Childbirth*. 2021;**21**(1):636.
 26. Maeda Y, Nakamura M, Ninomiya H, Ogawa K, Sago H, Miyawaki A. Trends in intensive neonatal care during the COVID-19 outbreak in Japan. *Arch Dis Child Fetal Neonatal Ed*. 2021;**106**(3):327–9.
 27. Rakuten Insight Inc. Domestic panels: [cited 2022 Feb 19]. Available from: <https://insight.rakuten.co.jp/member/>.
 28. The National Statistics Center e-Stat: population and population index. 2020: [cited 2021 Feb 6]. Available from: <https://www.e-stat.go.jp/dbview?sid=0003411191>.
 29. Streuling I, Beyerlein A, Rosenfeld E, Hofmann H, Schulz T, von Kries R. Physical activity and gestational weight gain: a meta-analysis of intervention trials. *BJOG*. 2011;**118**(3):278–84.
 30. Aune D, Sen A, Henriksen T, Saugstad OD, Tonstad S. Physical activity and the risk of gestational diabetes mellitus: a systematic review and dose-response meta-analysis of epidemiological studies. *Eur J Epidemiol*. 2016;**31**(10):967–97.
 31. Aune D, Saugstad OD, Henriksen T, Tonstad S. Physical activity and the risk of preeclampsia: a systematic review and meta-analysis. *Epidemiology*. 2014;**25**(3):331–43.
 32. Aune D, Schlesinger S, Henriksen T, Saugstad OD, Tonstad S. Physical activity and the risk of preterm birth: a systematic review and meta-analysis of epidemiological studies. *BJOG*. 2017;**124**(12):1816–26.
 33. The National Statistics Center e-Stat: area dimension and population density: whole country and prefectures. 2020: [cited 2021 Aug 25] Available from: <https://www.e-stat.go.jp/dbview?sid=0003411212>.
 34. Kyrklund-Blomberg NB, Granath F, Cnattingius S. Maternal smoking and causes of very preterm birth. *Acta Obstet Gynecol Scand*. 2005;**84**(6):572–7.
 35. Soneji S, Beltrán-Sánchez H. Association of Maternal Cigarette Smoking and Smoking Cessation with Preterm Birth. *JAMA Netw Open*. 2019;**2**(4):e192514.

Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1 Associations of delivery date with threatened abortion, threatened premature labor, and preterm birth

Table S2 The percentage of preterm birth among women who had threatened abortion or premature labor