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Original Article

Medical care of newborns born to mothers with confirmed or suspected severe acute respiratory syndrome coronavirus 2 infections in Japan

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Abstract *Background*: There are currently no definitive guidelines regarding newborns born to mothers with confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. This study aimed to investigate the medical care and management that provided or would provide for such newborns.

Methods: A web survey was conducted between September and October 2020. A total of 624 hospitals, which generally accept pregnant women for delivery, were involved in this study. The survey included the number of newborns born to mothers with confirmed SARS-CoV-2 infection and evaluated policies regarding the medical care and management of newborns born to mothers with confirmed or suspected SARS-CoV-2 infection.

Results: Pregnant women with confirmed or suspected SARS-CoV-2 infection were accepted or planned to be accepted in 54% (334) of the hospitals. Out of 52 newborns born to mothers with confirmed SARS-CoV-2 infection, SARS-CoV-2 RNA was detected from the nasopharyngeal swab of one newborn shortly after birth. The types of personal protective equipment during the delivery, the separation of the newborns from the mothers, the SARS-CoV-2 testing methods, and the use of incubators during the quarantine period were uniformly provided. However, the methods of ventilator treatment in the event of respiratory disorders, feeding during maternal isolation, and dequarantine and discharge criteria varied.

Conclusions: This survey demonstrated that one newborn detected a SARS-CoV-2 RNA shortly after birth out of 52 newborns who were born to mothers with confirmed SARS-CoV-2 infection. The policies regarding medical care and management for these newborns in Japan were provided.

Key words breast milk, coronavirus disease 2019, infection, newborn, pregnancy.

Coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in December 2019. The SARS-CoV-2 epidemic began in Japan in March 2020 and the number of patients with SARS-CoV-2 infection increased, mainly involving adults.¹ As the impact of the SARS-CoV-2 on newborns was unknown during the first and second waves from April to May and from July to August 2020, respectively, many facilities in all regions in

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Japan that would accept newborns born to mothers infected with SARS-CoV-2 and would perform neonatal care were prepared with strict infection control measures based on the tentative information and guidance provided by the Japan Society for Neonatal Health and Development, Centers for Disease Control and Prevention, or the American Academy of Pediatrics.^{2–4} As a result, a certain number of newborns born to mothers with confirmed or suspected SARS-CoV-2 infection were managed in Japan; it indicated that there was an increased burden on neonatal medical care and management in clinical practice. We should consider both the vertical SARS-CoV-2 infection from a mother with COVID-19 to the newborn as well as the horizontal contact or droplet SARS-CoV-2 infection by contact between the mother and the newborn or the newborn and the medical care staff.²⁻⁴ However, to date, globally, there have been no definitive guidelines addressing this situation.

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This study aimed to determine the positivity rate of SARS-CoV-2 RNA tests in newborns shortly after birth, born to mothers with confirmed SARS-CoV-2 infection, as of the end of August 2020, to investigate the medical care and management provided or would provide for newborns born to mothers with suspected or confirmed SARS-CoV-2 infection, based on the experience garnered during the first and second waves of the epidemic, and to make comparisons among primary delivery handling facilities, regional (secondary) and general (tertiary) perinatal medical centers.

Methods

Survey methods and ethics

The survey, using a dedicated website, was conducted by the neonatal medicine committee of the Japan Pediatric Society,⁵ from September 1 to October 8, 2020, when the second wave of the epidemic in Japan was subsiding. Letters were sent by mail to the heads of the pediatric departments at 2,507 hospitals in Japan requesting that the online survey be completed, including the uniform resource locator and the quick response code. The respondents answered using the website. This study was approved by the ethics committee of the Japan Pediatric Society (number: 2020-12, approved on August 14, 2020). The requirement for formal informed consent was waived because the data were anonymized and generated from regular practice without any personal information. The objectives of the survey were explained to the respondents on the request letters. The respondents were asked at the beginning of the survey if they consented to answer.

Respondents and health care facility classifications

The survey website was accessed by 1,890 pediatricians at hospitals. A total of 1,335 responses were obtained. Eight hospitals without the requisite consents and 203 hospitals with duplicated answers were excluded; therefore, 1,124 hospitals remained. Of these, 624 (56%) hospitals, where pregnant women are generally accepted for delivery, were finally enrolled and analyzed in this study. The enrolled hospitals were classified based on the three categories specified by the Japan Society of Perinatal and Neonatal Medicine (general perinatal medical centers: 102; regional perinatal medical centers: 207; primary delivery handling facilities: 315).⁶

Content of the survey

The survey contained questions regarding the current status or policy of medical care and management of newborns born to mothers suspected or confirmed with SARS-CoV-2 infection. The specific items were: (i) the acceptance of pregnant women suspected or confirmed with SARS-CoV-2 infection; (ii) the number of the newborns with positive SARS-CoV-2 RNA tests shortly after birth; (iii) delivery and neonatal resuscitation, and (iv) medical care and management of the newborns (locations and negative pressure private rooms, treatments for the newborns with respiratory disorders, SARS-CoV-2 testing, beds during the quarantine period and personal protective equipment (PPE) for medical staff, neonatal feeding while the infected mother was isolated, and de-quarantine and discharge criteria).

Statistical analysis

For statistical analysis, the Pearson's χ^2 test was performed for the m × n tables to compare the groups using Excel (Social Survey Research Information Co., Ltd., Tokyo, Japan). The Clopper–Pearson method was used for 95% confidence intervals. Statistical significance was set at P < 0.05.

Results

Acceptance of pregnant women suspected or confirmed with SARS-CoV-2 infection

Pregnant women suspected or confirmed with SARS-CoV-2 infection were accepted or planned to be accepted in 54% (334/624 hospitals), including 82 general perinatal medical centers (82/102, 80%), 151 regional perinatal medical centers (151/207, 73%), and 101 primary delivery handling facilities (101/315, 32%) with a statistically significant difference (P < 0.0001). The general perinatal medical centers exhibited a high acceptance rate of pregnant women suspected or confirmed with SARS-CoV-2 infection (P < 0.0001, Table 1).

Positivity rates of SARS-CoV-2 RNA tests in newborns shortly after birth

By August 31, 2020, a total of 52 newborns were born to mothers with confirmed SARS-CoV-2 infection at 31 hospitals. Forty-six (88%) were in 13 special alert prefectures: Tokyo, Osaka, Hokkaido, Ibaraki, Saitama, Chiba, Kanagawa, Ishikawa, Gifu, Aichi, Kyoto, Hyogo, Fukuoka; SARS-CoV-2 RNA was detected in one newborn by a real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test using a nasopharyngeal swab (1.9%, 95% confidence interval: 0.0–10.3%).

The 31 hospitals (9% of the 334 hospitals) managed newborns born to mothers with confirmed SARS-CoV-2 infection, including 13 general perinatal medical centers (13/82, 16%), nine regional perinatal medical centers (9/151, 6%), and nine primary delivery handling facilities (9/101, 9%; P = 0.08).

Delivery and neonatal resuscitation

Of the 324 hospitals that either accepted or planned to accept pregnant women with SARS-CoV-2, the selected delivery modes were vaginal delivery and cesarean section in 33% and 67%, respectively. Vaginal delivery was more common at primary delivery handling facilities than at general or regional perinatal medical centers (P = 0.034, Table 1). The PPE that was used or planned to be used by the attending neonatologist or pediatrician to receive the newborn, in >90% of hospitals

Table 1 Comparison among the groups

	Number of hospitals		Only pregnant women following-up in the hospital			Any pregnant women				P value	
Group			n		%		n	%			
A. Acceptance of pregnant women wit General perinatal medical center Regional perinatal medical center Primary delivery handling facility Total	h confirmed or suspected 82 151 101 334	SARS-C	CoV-2 info 12 35 55 102	ection	15 23 55 31		70 116 46 232	85 77 46 70		<0.0001	
	Number of hospitals			Vaginal delivery			Cesarean section			P value	
Group			n		%		п	%	,		
B. Delivery mode General perinatal medical center Regional perinatal medical center Primary delivery handling facility Total	80 144 100 324		18 48 42 108		23 33 42 33		62 96 58 216	78 67 58 67	3 7 3	0.034	
	Number of hospitals		Е	Existence			Abse	nce		P value	
Group			n	0%		n					
C. Negative pressure private room General perinatal medical center Regional perinatal medical center Primary delivery handling facility Total	80 144 100 324		58 54 17 129		73 38 17 40		22 90 83 195	28 63 83 60		<0.0001	
	Number of hospitals Numb hospita respir supp		er of <i>P</i> value ls for atory port		Respira- tory venti- lation by tracheal intubation without NPPV		NPPV before tra- cheal intu- bation		P value		
Group		n	%			n	%	n	%		
D. Supports for the newborns with resp General perinatal medical center Regional perinatal medical center Primary delivery handling facility Total	piratory disorders 80 144 100 324	80 111 19 210	100 77 19 65	<0.00	01*	50 54 6 110	63 49 32 52	30 57 13 100	38 51 68 48	0.053	
	Number of hospitals	Formula milk		Expressed breast milk		Breast milk directly from infected mothers wearing PPE		Donor breast milk		<i>P</i> -value	
Group		n	%	n	%	n	%	n	%		
E. Feeding while the infected mother v General perinatal medical center Regional perinatal medical center Primary delivery handling facility Total	was isolated 63 125 81 269	39 64 37 140	62 51 46 52	22 55 34 111	35 44 42 41	1 6 10 17	2 5 12 6	1 0 0 1	2 0 0 0	0.238**	

n, number; NPPV, noninvasive positive pressure ventilation; PPE, personal protective equipment; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2. *Compared the number of hospitals provided or planned to provide respiratory support among the facilities. **Compared the number of hospitals provided or planned to provide each feeding type among the facilities.



Fig. 1 Personal protective equipment that used or planned to use by an attending neonatologist or pediatricians to receive the newborn at the delivery. The *Y*-axis shows the percentage of the 324 hospitals. The number of hospitals has also been added.

consisted of gloves, standard gowns, caps, N95 masks, and face shields (Fig. 1).

Resuscitation of newborns was performed or was planned to be performed with an infant warmer in the usual delivery room in 60% of the 324 hospitals, with an incubator in the same delivery room in 12%. They were immediately moved to another room in 28%. In 322 respondent hospitals, 73% percent wiped off amniotic fluid at birth in the usual manner, 19% rinsed with warm saline, and 8% by other means.

Medical care and management of the newborns

Locations for care and negative pressure private rooms

In most of the 328 hospitals, newborns were either separated or there was a plan to separate the newborn from the infected mother, rather than the newborn remaining in a private room shared with the infected mother wearing PPE (Fig. 2a). Of the 306 hospitals with separation from the infected mother, the main locations for caring for the newborns without respiratory disorders were the neonatal intensive care units, growing care units, and obstetric well-newborn rooms (Fig. 2b). Forty percent of the hospitals possessed negative pressure private rooms. Negative pressure private rooms were more common in general perinatal medical centers than at the other institutions (P < 0.0001, Table 1).

Support for the newborns with respiratory disorders

If the newborn developed respiratory distress after birth, 65% of the 324 hospitals provided or planned to provide respiratory support with oxygen, such as respiratory ventilation with tracheal intubation and noninvasive positive- pressure ventilation

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(NPPV). All the general perinatal medical centers (100%) could provide respiratory support with oxygen. When respiratory support was required, 52% and 48% of the hospitals made or planned to make respiratory ventilation by tracheal intubation without NPPV and NPPV before tracheal intubation, respectively (Table 1).

SARS-CoV-2 testing

Importantly, 320 (99%) of the 324 hospitals either tested or planned to perform SARS-CoV-2 testing for newborns. Testing for SARS-CoV-2 RNA was selected by all hospitals (320/320, 100%), such as RT-PCR or loop-mediated isothermal amplification. Eighty-one hospitals (81/320, 25%) also tested or planned to test for SARS-CoV-2 antigens. Materials for testing were nasopharyngeal swabs in 99%, stool in 13%, and saliva in 3% of the 320 hospitals. The greatest testing frequency was twice, in 61% of the hospitals. Meanwhile, 15% of the hospitals were "unknown" (Fig. 3a). The most common age for the scheduled test was day 0 in 88% of the hospitals (Fig. 3b).

Bathing

Thirty-one percent of the 324 hospitals performed or planned to perform usual bathing at the age of 1 day, 32% within 24 h, and 37% did not perform or plan to perform bathing until the release of the newborns from isolation.

Beds during the quarantine period and PPE for medical staff

For newborns without respiratory disorders during the quarantine period, 301 (93%) of the 322 hospitals kept or planned to



Fig. 2 Locations (a) and the detailed place (b) to give medical cares and managements for the newborns. GCU, growing care unit; NICU, neonatal intensive care unit; PPE, personal protective equipment.



Fig. 3 The frequency (a) and scheduled days of age (b) for the SARS-CoV-2 testing *Y*-axis of (b) shows the number of hospitals. The percentages were also added. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

keep the newborns in an incubator, and 21 (7%) placed or planned to place the newborns on cots with >2 m distances from the other newborns. Figure 4 shows the PPE for medical staff to utilize when performing medical care during the quarantine of newborns. Most hospitals used or planned to use N95 masks or surgical masks, gloves, gowns, caps, and face shields.

Neonatal feeding during isolation of the infected mother

Formula milk was used, or its use was planned, for feeding newborns only during the period of isolation of the infected mother; subsequently, expressed breast milk was given, followed by breast milk directly from infected mothers wearing PPE (Fig. 5), without significant differences between the groups (P = 0.238, Table 1).

De-quarantine and discharge criteria

Two major de-quarantine criteria were as follows: after confirmation of a negative result for the SARS-CoV-2 test and completion of the health observation period (14 days after birth, 40%), and after confirmation of a negative result for the SARS-CoV-2 test (37%). The discharge criteria were the same as usual if a negative result for the SARS-CoV-2 test was confirmed (61%), followed by discharge after the end of the observation period (39%, Fig. 6).



Fig. 4 Personal protective equipment that used or planned to use by medical staffs to give medical cares during the quarantine of newborns. The *Y*-axis shows the percentage of the 322 hospitals. The number of hospitals has also been added.



Fig. 5 Feeding while the infected mother was isolated for the newborns. PPE, personal protective equipment.

Discussion

From September to October 2020, ~80% and 70% of general and regional perinatal medical centers, respectively, had already made preparations for the medical care and management of newborns born to mothers with suspected or confirmed SARS-CoV-2 infection, suggesting that many perinatal centers in Japan accepted or planned to accept such mothers and newborns. The reasons may be that most of the perinatal medical centers in Japan are located at the large hospitals in the regions, where adult patients with COVID-19 are accepted, and they also fulfill a role as perinatal medical centers. The Centers for Disease Control and Prevention has reported that vertical transmission is rare or uncommon, although concerns about possible intrauterine or intrapartum transmission have been raised.³ Indeed, the American Academy of Pediatrics and Japanese Society for Neonatal Health and Development has reviewed the literature and reported vertical infection rates of 1–3% and 0–4.7%, respectively.^{2,4} A systematic review using case reports and case series from various countries has reported 3–4%.^{7,8} In the present study, the rate was 1.9%, which was similar to these reports.

In the present study, a policy difference was observed in the methods of respiratory support for newborns with respiratory disorders between respiratory ventilation by tracheal intubation without NPPV and NPPV before tracheal intubation. Some neonatologists or pediatricians may consider that because aerosol infection is a transmission route of SARS-CoV-2, respiratory ventilation by tracheal intubation may pose a lower risk of aerosol infection, although both methods of support induce aerosols.⁹ These supportive methods would be provided in a negative pressure private room if possible and the staff should wear full PPE, including N95 masks and eye protection equipment (face shields or goggles). This survey showed that ~70% of general perinatal centers in Japan have negative pressure private rooms.

The main kinds of feeding while the mother was in isolation were expressed breast milk and formula milk. In only 6% of the hospitals were the newborns given, or was it planned to give them, breast milk directly from infected mothers wearing PPE. The number of hospitals where the newborns and the infected mother with PPE shared or planned to share a private room was also extremely limited. Immediately after the start of the SARS-CoV-2 epidemic, the American Academy of



Fig. 6 De-quarantine (a) and discharge criteria (b) of the newborns.

Pediatrics recommended that newborns should be separated from infected mothers because the situation was unknown; however, they currently report that the SARS-CoV-2 transmission rate from the infected mother to newborns did not increase if the infected mother observed appropriate infection control measures.⁴ The American Academy of Pediatrics and the Japanese Society for Neonatal Health and Development also have stated that there is no need to withhold breast milk because there have been no reported cases of breast milkacquired SARS-CoV-2 infection,^{2,4} although there are some reports that SARS-CoV-2 RNA was detected in breast milk.^{8,10,11} In a systematic review by Walker et al.,⁷ no difference was found in the infection rate in the newborns fed with breast milk and those fed with formula milk, and whether newborns were kept in the same room with the infected mothers or were separated from the infected mothers. At present, in Japan, because the infected mothers with SARS-CoV-2 need to be isolated, the newborns cannot be in the same room with the mothers and cannot breastfeed directly.

In some hospitals, the end of the health observation period (14 days after birth) was a criterion for the de-quarantining and discharge of the newborns, in addition to the confirmation of negative SARS-CoV-2 test results. The reason might be that the newborns are considered to have been in close contact with SARS-CoV-2 *in utero* or during the intrapartum.

This study has some limitations. At the time of this survey, only 31 hospitals experienced the actual delivery of pregnant women with confirmed SARS-CoV-2 infection; therefore, most of the hospitals responded to the assumed policies regarding the medical care and management that would provide for newborns born to mothers with suspected or confirmed SARS-CoV-2 infection. Nationwide surveys for the actual medical care and management that provided for these newborns should be performed in the near future (e.g. the actual number of hospitals that gave expressed breast milk). Second, one newborn detected a SARS-CoV-2 RNA by RT-PCR. As it might be a false-positive result, it is necessary to perform not only

SARS-CoV-2 RT-PCR tests using neonatal and maternal materials, such as amniotic fluid, placenta, neonatal nasopharyngeal and anal swabs, and blood, but also serological tests for SARS-CoV-2 IgG and IgM using the umbilical cord and neonatal blood from newborns to prove vertical SARS-CoV-2 infection from a mother with COVID-19 to the newborn.¹² Finally, the number of hospitals analyzed was only 1124. However, this included 102 general perinatal medical centers and 207 regional perinatal medical centers. Therefore, 94% of the 108 general perinatal medical centers in Japan were included. It could thus be assumed that many hospitals, where medical treatment and care for high-risk newborns are provided, would be covered.

Conclusion

This survey demonstrated that one newborn detected a SARS-CoV-2 RNA shortly after birth out of 52 newborns who were born to mothers with confirmed SARS-CoV-2 infection. The types of PPE used during delivery, the separation of newborns from the mothers, SARS-CoV-2 testing methods, and use of incubators during the quarantine period were uniformly provided. However, the methods of ventilatory treatment in the event of respiratory disorders, feeding during the maternal isolation, and the de-quarantine and discharge criteria varied.

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Disclosure

The authors declare no conflict of interest.

Author contributions

All authors contributed to the intellectual content of this manuscript. I.M. wrote the first draft of this manuscript. I.M. and S.T. designed this study. I.M. collected the data. I.M. performed statistical analyses. S.T., T.K., K.W., and K.M. revised the work critically for important intellectual contents and all authors approved the final version of this work.

References

- 1 Tokyo Metropolitan Government. Updates on COVID-19 in Tokyo. [Cited 2021 March 23]. Available from: https://stopc ovid19.metro.tokyo.lg.jp/en/
- 2 Japanese Society for Neonatal Health and Development. Recommended measures on newborn infants born to mothers with suspected or confirmed the new coronavirus infection. [Cited 2021 March 23]. Available from: http://jsnhd.or.jp/pdf/ COVID19JSNHD20201019.pdf
- 3 Centers for Disease Control and Prevention. *Evaluation and management considerations for neonates at risk for COVID-19* (Updated Dec. 8, 2020). [Cited 2021 March 23]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/caring-for-newborns.html

- 4 American Academy of Pediatrics. FAQs: Management of infants born to mothers with suspected or confirmed COVID-19. [Cited 2021 March 23]. Available from: https://services.aa p.org/en/pages/2019-novel-coronavirus-covid-19-infections/ clinical-guidance/faqs-management-of-infants-born-to-covid-19-mothers/
- 5 Morioka I, Toishi S, Kusaka T *et al.* Survey on the medical cares and managements for newborns born to pregnant women with confirmed or suspected severe acute respiratory syndrome coronavirus 2 infection (summary). *J. Jpn. Pediatr. Soc.* 2021; In press. (In Japanese)**125**: 844–5.
- 6 Japan Society of Perinatal and Neonatal Medicine. *Training hospitals for neonatologists*. [Cited 2021 March 23]. Available from URL: http://www.jspnm.com/Senmoni/ShisetsuS.aspx. (In Japanese)
- 7 Walker KF, O'Donoghue K, Grace N *et al.* Maternal transmission of SARS-COV-2 to the neonate, and possible routes for such transmission: A systematic review and critical analysis. *BJOG* 2020; **127**: 1324–36.
- 8 Rodrigues C, Baía I, Domingues R, Barros H. Pregnancy and breastfeeding during COVID-19 pandemic: A systematic review of published pregnancy cases. *Front. Public Health* 2020; 8: 558144.
- 9 Hosono S, Isayama T, Sugiura T *et al*. Management of infants born to mothers with suspected or confirmed SARS-CoV-2 infection in the delivery room: A tentative proposal 2020. *Pediatr. Int.* 2021; **63**: 260–3.
- 10 Groß R, Conzelmann C, Müller JA *et al.* Detection of SARS-CoV-2 in human breastmilk. *Lancet.* 2020; **395**(10239): 1757–8.
- 11 Chambers C, Krogstad P, Bertrand K *et al.* Evaluation for SARS-CoV-2 in breast milk from 18 infected women. *JAMA* 2020; **324**: 1347–8.
- 12 Hijikata M, Okahashi A, Morioka I. Vertical transmission of severe acute respiratory syndrome coronavirus 2 from the mother to the infant. *JAMA Pediatr.* 2020; **174**: 1006–7.