COVID-19: a systematic review of perinatal case series up to April 5, 2020

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This communication consists of two tables from systematic reviews. They are from peer reviewed guidelines in Swedish about COVID-19 (infection with the corona virus SARS-CoV-2), published by www.internetmedicin.se. Their guidelines are not official but highly regarded and much used. My guidelines are compatible with official guidelines, if they exist. Unfortunately, my English is not revised by a translator.

Literature was searched up to April 5, 2020. PubMed was searched for "Covid-19 and pregnancy" and "Covid-19 and child*". Studies that contained clinical data on mothers and/or newborn babies were selected for inclusion in my review. The reference lists of the selected studies and of review articles were also searched.

Summary of Table 1: Outcome of pregnancies complicated with maternal COVID-19

In 3 cases, symptoms of maternal COVID-19 didn't appear until the first days after delivery.

Countries: China, Iran and South Korea

Number of deliveries: 130 (vaginal 31, section 96, unknown 3)

Number of live newborns: 129 (one pair of twins, one miscarriage, one child death due to multiple organ failure)

Length of pregnancy at delivery: 25-41 weeks (most newborns were term)

Seriously ill or dead mothers: One mother was treated with ECMO at time of publication (Liu Y, Chen H 2020). To mothers in Iran died in ARDS after delivery; details were not published (Karimi-Zaorchi 2020).

Seriously ill or dead newborn babies: Data in Table 1 indicate that COVID-19 in pregnant women usually has benign courses for mothers and children, at least after infections in the third trimester. However, one pregnancy ended with a miscarriage (Liu Y, Chen H 2020). One child, born after 34 weeks + 5 days, died 9 days old of DIC and MODS. The mother caught fever 3 days after delivery and the child became ill the day before death. The authors mention viremia but it is unclear if it is a finding or a hypothesis. (Zhu 2020)

Vertical transmission: in 19 newborns, viral tests were collected from nasopharynx and/or throat and in another 50 newborns, viral tests were collected from e.g. amnion fluid, umbilical cord, breastmilk, placenta and in most cases also from nasopharynx and/or throat. Four nasopharynx swabs were positive for COVID-19-virus at age 2-3 days. These infants had breathing difficulties but both mothers and infants recovered without problems.

A positive COVID was collected from a newborn in London a few minutes after birth but it was not known if virus hade infected the baby *in utero* or in the vagina (Murphy 2020).

Two of 6 newborns delivered by mothers who were moderately ill in COVIR-19 had high titers of IgM antibodies for COVIR-19-virus. “M” in IgM means “macro”, i.e. the molecule is not usually transferred from mother to fetus because of its size. It is therefore possible that virus has penetrated the fetus and stimulated its production of IgM. This was supported by an increase of interleukin-6 as a sign of infection. The infants were fine with no sign of illness. (Zeng H 2020) Another infant had also high levels of IgM for COVID-19-virus and interleukins 2 hours after birth (Dong L 2020).

Table 1. Outcome of pregnancies complicated with maternal COVID-19

Reference	**Number of pregnancies /sectio (CS)**	**Gestational age at illness onset (weeks)**	**Complications during pregnancy (in addition to maternal COVID-19)**	**Deaths in mother/child; complications after discharge**	**Vertical transmittance of virus**
Chen H	9/9	36-39	Fetal distress, PROM, hypertonia, pre-eclampsia, influenza	0/0; no complications	No (6 children tested)
Chen S	5/2	38-40	Gestational diabetes (2 mothers), preeclampsia (1), fetal tachycardia (1)	0/0; excellent clinical course	No? (discrepancy between text and table)
Dong L	1/1	34+2 (CS 37+6)	No	0/0	Yes? 2h after birth, the baby’s blood contained IgM for SARS-CoV-2
Fan	2/2	≥36	No maternal or infant complications	0/0	No (7 different tissues examined in each baby)
Karimi-Zarchi	3/?	?		2/0 two mothers die of ARDS	No
Lee	1/1	36+2	Cephalo-pelvic obstruction	0/0	No
Liang cites unknown researcher	18/2 (i.e. 16 PN)				No

Liu D	11/10		No complications	0/0	Unknown
Liu W	3/2	38-40	One fetus had fetal distress and chorioamnionitis	0/0	No
Liu Y	10 CS; 3 healthy, on-going pregnancies	25-38	5 emergency CS due to fetal distress (3 cases), PROM (1), stillbirth (1). The 9 live born babies had Apgar 1' =10.	0?/1. One mother in ECMO at time of publication, after MODS, ARDS and septic shock.	No
Wang	1/1	30	Severe maternal pneumonia; pathological CTG	0/0 (mother and baby well after delivery)	No
Wen	0/0 (ongoing pregnancy)	30	No complications so far. COVID-19 healed after treatment with interferon.	The baby was not born at time of publication	Unknown
Yu	7/7	37-41	Influenza, Legionella	0/0; no complications except SARS-CoV-2 (see right)	3 infants tested; 1 had SARS-CoV-2 virus and mild respiratory signs when 36 hours old; follow-up uneventful
Zeng	33/26	4 preterm babies	No	0/0; 2 term infants had lethargy, fever and pneumonia; one preterm (31w+2d) had fetal distress, RDS, DIC and sepsis. Follow-up was uneventful.	The 3 sick infants (see left) had SARS-CoV-2 in nose and anus when 2 days old. No data on virus in the other 30 infants.
Zhang, cited by Schwartz	16/16	35-41	Normal rate of complications		No (negative throat swabs in 10 babies)

Zhu	9/7 (10 babies)**	31-39; 6 babies were preterm	Fetal distress (6 cases). One child died of MODS.	0/1	No (negative pharyngeal swabs in 9 babies)

Abbreviations: ARDS, acute respiratory distress syndrome; CS, caesaren section; ECMO, extracorporeal membrane oxygenation; MODS, multiple organ dysfunction syndrome; pp, post partum; PN, partus normalis (normal, vaginal delivery); PROM, premature rupture of membranes.

*In most cases, the pregnant woman delivered within one week after the beginning of COVID-19 symptoms. **In 3 cases, the women became sick in COVID-19 1-3 days after delivery.

Deleted studies

Liu H 2020: Very few clinical data.

Review which have been reviewed for missed primary studies

Panahi (2020)

Table 2. Case– fatality rate (%) for reported COVID–19 cases, by age group, in 5 countries. Data were collected up to the following dates: China 11 February 2020, Italy 2 April, South Korea 5 April, Sweden 7 April and the USA 16 March.

	China		Italy		South Korea		Sweden		USA
Age (years)	No. of deaths	CFR	No. of deaths	CFR	No. of deaths	CFR	No. of deaths	CFR	CFR
0-9	0	0	0	0	0	0	0	0	0**
10-19	1	0,2	0	0	0	0	0	0	0**
20-29	7	0,2	6	0,1	0	0	3	0,5	20-44: 0,1
30-39	18	0,2	29	0,4	1	0,1	1	0,1	
40-49	38	0,4	110	0,8	2	0,2	2	0,2	45-54: 0,5
50-59	130	1,3	479	2,3	13	0,7	26	1,9	55-64: 1,4
60-69	309	3,6	1 448	8,0	25	1,9	41	3,8	65-74: 2,7
70-79	312	8,0	4 196	21,8	51	7,5	156	14,0	75-84: 4,3
≥80	208	14,8	5 029	30,5	91	19,7	362	21,4	≥85: 10,4
All ages	1 023 (2611 on March 27, 2020)*	2,3	12 550	11,8	183	1,8			1,8

CFR, case fatality rate. Source: CCDC 2020; ISS (2020); KCDC (2020); CDC-MMWR (2020). *National Health Commission of the People's Republic of China. **CDC declared on April 6 that 3 children were reported dead by COVID-19 and CDC was investigating the cases.

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