Infection of SARS-CoV-2 (COVID-19) – a guide for clinicians

Indications for the care of the pregnant women and the newborn, including the management of childbirth and considerations for breast feeding

THE FOLLOWING IS AN ITALIAN APPROVED PROTOCOL PREPARED BY EXPERTS IN OBSTETRICS, NEONATOLOGY, MIDWIFERY, ANESTHESIOLOGY, INFECTIOUS DISEASE, MICROBIOLOGY, VIROLOGY AND PATHOLOGY LED BY PROF GIAN CARLO DI RENZO, UNIVERSITY OF PERUGIA (See panel at the end for full details)

This document has been prepared by a panel of experts (via e-conferencing) drawing on guidance from documents provided by the Italian National Institute of Health and two Scientific Societies (SIMP Italian Society of Perinatal Medicine, SIN Italian Society of Neonatology) as well as taking into account the scientific and epidemiological data currently available, including the recent guidelines of the Royal College of Obstetricians and Gynaecologists (13/3/2020) and of the CDC of Atlanta (USA) - and also with the approval of the Provincial Orders of the Midwifery Profession (of Perugia and Terni)
This guidance is subject to future change and updating based on the continuing acquisition of knowledge about the epidemic of SARS-CoV-2, about its perinatal transmission and about the clinical characteristics of cases of infection in pregnancy and in the neonatal period.

Glossary:

We want to clarify the meaning that some terms have in this document:
- SARS-CoV-2 means the possible viral causative agent responsible for SARS, also called Wuhan's new nCoV-2019 coronavirus.
- SARS stands for Severe Acute Respiratory Syndrome from coronavirus 2, acronym from the English Severe Acute Respiratory Syndrome.
- COVID-19 (Coronavirus Disease-2019) means the SARS-CoV-2 disease identified at the end of 2019 in the Wuhan region of PR China.

1) Premise

The recent epidemics from the newly isolated coronavirus in Wuhan (China) at the end of 2019 (SARS-CoV-2) in addition to other clinical and public health problems, also raises issues regarding the organization of the local networks (in our case, the Umbria Perinatal Network) in relation to the management of the infection in pregnancy, the possible maternal-infant transmission of the infection before, during and after childbirth and also the safety of the joint management of the newborn and the opportunity of breastfeeding: the object of this document is to try and clarify these..

2) Limits of current knowledge

The SARS-CoV-2 virus spreads mainly via person to person through close contact (0-2 meters) and it is transmitted through “flugge”, the droplets of the respiratory tract when an infected individual sneezes or coughs.
It is not yet clear what may be the impact of a possible perinatal transmission of SARS-CoV-2 infection whose outcome – but drawing the analogy with past SARS-CoV-1 (Severe Acute Respiratory Syndrome) and MERS-CoV epidemics (Middle East Respiratory Syndrome Coronavirus) it could depend more on the severity of the maternal infection and on concomitant obstetric pathologies rather than on the SARS-CoV-2 infection itself.
Any neonatal SARS-CoV-2 infection could be the result of a transmission acquired by the mother's respiratory tract in the puerperium rather than transplacentally.

3) Pregnancy and birth

- Pregnant women are generally at greater risk of developing respiratory tract infections that may have potentially more serious implications - and therefore they need appropriate care when they present at health facilities with respiratory symptoms;
- The General Emergency Department of each hospital with a maternity ward must provide a triage area for pregnant women, guaranteeing a place of isolation (room with bathroom) and trained personnel, equipped with individual prevention devices, IPD *(Individual Protective Devices)*
- A nasopharyngeal swab from the pregnant woman with suspected COVID-19 infection should be performed in accordance regional protocols in case of:
a) acute respiratory syndrome associated with risk regarding geographical origin or contact with an infected person; and,
b) all pregnant women with a clinical picture suggestive of respiratory infection who need hospitalization, regardless of the aforementioned conditions.
In particular, for pregnant women, the locally applicable criteria defined for the early identification and management of sepsis should be followed in the presence of fever ≥ 37.5 ° C and / or cough and with respiratory symptoms, acute onset, associated with dyspnoea, (which is defined as oxygen saturation ≤ 95% and / or respiratory rate> 20 acts / minute -MEOWS criteria);
- Taking into consideration the limit of current knowledge on COVID-19 infection in the maternal-neonatal environment and the need to guarantee safety and continuity of assistance for the pregnant woman before and during childbirth with dedicated care pathways (with a rational use of resources), it is considered appropriate to provide for the admission and care of a positive pregnant woman, who need hospitalization and to refer her to a limited number of Hub Centers.

4) Suspicious cases and transportation issues

- Pending confirmation of the laboratory tests, suspicious cases should be managed by the unit to which the pregnant woman is admitted, identifying a place of isolation (room with bathroom) where the pregnant woman is assisted by trained health professionals equipped with IPD. In the event that the swab turns out to be positive, in the absence of contraindications to travel, the patient should be transferred to one of the appointed Reference Centers and she should be admitted to an Infectious Diseases Department with 24/7 consultancy by the obstetric staff .
- An Assisted Maternal Transport Service (STAM) should be used in accordance with the rules established by the service and the current protocols for COVID-19 infection. Therefore, the peripheral hospital to which any pregnant woman found positive may access, should contact

the appointed Reference Centers directly and the transport should be carried out by the team of the peripheral unit. The patient must wear the surgical mask and all the IPD, provided for the protection against contagion for the health personnel must be put in place.

5) Care pathway (see also Table 1)

- Each maternity hospital should prepare a care pathway for the management of suspected or confirmed cases that provides for appropriate obstetric assistance at delivery for any situations in which there is a contraindication to the transfer of the pregnant woman. In particular, the pathway for obstetric assistance for vaginal delivery or cesarean section and for the puerperium, which includes the protection of health workers, should consider the recommendations listed in Table 1.

Based on current knowledge and on the results of the only study carried out in China (in which the presence of SARS-CoV-2 in umbilical cord blood, amniotic fluid and breast milk was not demonstrated), there is no elective indication for cesarean section in women with COVID-19 infection and the current indications for cesarean section remain valid. Considering also that cesarean section represents an independent risk factor for maternal mortality, it is appropriate to carefully evaluate this method of delivery in pregnancies affected by COVID-19.

- However, if the pregnant woman is symptomatic, the risks / benefits of proceeding as soon as possible in performing cesarean section (maximum 37 weeks completed if elective) should be evaluated in order to allow better control of lung function and also the possible administration of antivirals and anti-citokines agents (like tocilizumab) of which the pharmacodynamics in pregnancy and the risks for the fetus-newborn are largely unknown.

6) Withdrawals and sampling (see also Appendix)

- For all pregnant women who tested positive to SARS –CoV-2 , the following biological materials should be collected at birth:
• Oropharyngeal swabs as well as vaginal, rectal, placental swabs; Maternal and cord serum; Breast milk (after colostrum)
• Biopsy and conservation of fetal membranes and placenta , for possible analysis at the Pathology Department.
- For the newborn the following biological material should be collected:
• nasopharyngeal swab for rt-PCR for 2019 nCoV

7) Postpartum mother and newborn (seeTable 2, Figure 1)

- Whenever possible, the preferred option is for the joint management of mother and infant, in order to facilitate interaction and the initiation of breastfeeding. This choice is feasible when a mother previously identified as SARS-CoV-2 positive is asymptomatic or is on the way to recovery or when an asymptomatic or paucisymptomatic mother is proband for SARS-CoV-2;

- If the mother has a frankly symptomatic respiratory infection (with fever, cough and respiratory secretions), the mother and infant should be transiently separated, pending the response of the laboratory test (RNA-PCR) for coronavirus;

a) if the test is positive, mother and infant continue to be managed separately;

b) if the test is negative, rooming-in for mother-newborn is applicable, given the normal prevention of airborne respiratory diseases (mask etc).

- The decision regarding whether or not to separate mother and newborn must, however, be made for each individual pair taking into account the information/consent of the parents, the logistical situation of the hospital (see possibility of in-patient at the Department of Infectious Diseases) and possibly also the local epidemiological situation on the spread of SARS-CoV-2;

- In the event of the separation of the infant from the mother, the use of fresh expressed breast milk is recommended, while the pasteurization of breast milk is not indicated.

- In the event of a positive SARS-CoV-2 mother, rigorous measures must always be followed to prevent the possible transmission of the infection by air or by contact with the respiratory secretions. Therefore, the infant, other hospitalised patients and health personnel should be protected.

- The compatibility of breastfeeding with drugs possibly administered to women with COVID-19 must be assessed on a case-by-case basis.

(see also "Newborn path from positive / suspected positive mother for SARS-Cov-2" City Hospital of Terni on 14/3/2020 and "Pediatric / neonatal patient path COVID 19" prot 17037 on 11/3/2020 University Hospital of Perugia)

8) Use of breast milk

- Breastfeeding and the use of breast milk are recognized as having an important impact on maternal and child health, with further advantages at a family, social and economic level.

-In the event of a maternal infection with SARS-CoV-2, based on current scientific knowledge and by analogy with other known viral respiratory transmitted infections, breast milk is not currently considered to be a transmission vehicle. The current SARS-CoV-2 epidemic does, however, require the need to combine the promotion of breastfeeding with a correct hygienic-sanitary approach, which limits the contagion by air and by contact with the respiratory secretions of infected patients (including postpartum mothers)

- In the event of separation between the mother and the newborn, automatic recourse to breast milk substitutes should be avoided, rather implementing the expression of breast milk with the transport and administration of fresh breast milk to the infant.

- Expressed breast milk should not be pasteurized before being fed to the newborn, because, according to current knowledge, it does not represent a vehicle of infection.

- The use of SARS-CoV-2 positive mother's breast milk inside a Neonatal Intensive Care Unit follows specific protocols.

- In cases of serious maternal infection the expression of breast milk should not be carried out in view of the general condition of the mother.

9) SARS-CoV-2 positive infants admitted to NICU (Neonatal Intensive care Unit)

Newborns and infants weighing <5 kg with confirmed positivity for 2019-nCoV and the need for neonatal intensive care must be transferred to appropriate intensive care units using an Emergency Neonatal Transport System.

10) Communication-Information

Professionals must ensure to each woman / couple adequate forms of communication, which is both consistent and clear ; also in the face of the limited current knowledge they should share all the choices of the care pathway, thus ensuring their support.

Table 1: Indications for obstetric management in case of vaginal delivery

- consider obstetric assistance for vaginal birth as "assistance maneuvers that can produce aerosols": use FFP2 / FFP3 facial filters, disposable water-repellent TNT long-sleeved gown, double gloves, visor / goggles, disposable headgear, shoes and proceed for disposal in accordance with the appropriate standards

- there is no evidence of contraindications to peridural or spinal analgesia

- continuous CTG monitoring (given that a higher incidence of fetal distress in labor has been reported)

- perform early clamping of the cord (the double distal clamp and the double proximal clamp allows to have an intact cord section for sampling)

- do not aspirate with a suction device

- no skin to skin

- ensure the presence of the neonatologist at delivery

- no presence of father or family member at birth

- carry out checks on expected biological samples. (see Appendix)

Notes

Booth or pull curtain, surgical face mask to the mother when breastfeeding or in intimate contact with the newborn, careful washing of the hands, positioning of the newborn's cradle at a distance of 2 meters from the mother's head, forbidden visits of relatives and friends;
° In addition, adequate protection measures by healthcare personnel, according to Health Office indications;
^ Mother's fresh milk must be expressed with a dedicated manual or electric breast pump. The mother should always wash her hands before touching the bottles and all the components of the breast pump, following the recommendations for proper washing of the breast pump after each use.

Table 2. Indications for mother-infant management in the perinatal period (See Figure 1)

State of the mother	Execution in the mother of the RNA-PCR test for SARS-CoV-2 on pharyngeal swab	RAR-PCR test for SARS-CoV-2 on pharyngeal swab in newborn	Isolation of the mother °	Management of the newborn during the hospital stay °	Breastfeeding tips	Preventive measures on mother-infant infections
Asymptomatic or paucisymptomatic mother known to be SARS-CoV-2 positive	Already done	YES	YES, in a dedicated area (Inf Dis Dept)	In a rooming-in regimen, but in an isolated and dedicated area	YES	YES
Paucisymptomatic mother SARS-CoV-2 under investigation	YES	Only if positive maternal test	YES, in a dedicated and isolated area awaiting the result of the laboratory test	In a rooming-in regimen, but in an isolated and dedicated area, at least until the result of the laboratory test	YES	YES
Mother with symptoms of respiratory infection (fever, cough, secretions) with positive SARS-CoV-2 status or under investigation	YES or already in progress	Only if positive maternal test	YES, in a dedicated area awaiting the result of the laboratory test	Newborn isolated and separated from the mother, at least until the result of the laboratory test. It is admitted in a dedicated area of Neonatology (if asymptomatic) or of the NICU (if with respiratory pathology) with the possibility of isolation	NO; use of squeezed milk. Pasteurization is not indicated	YES

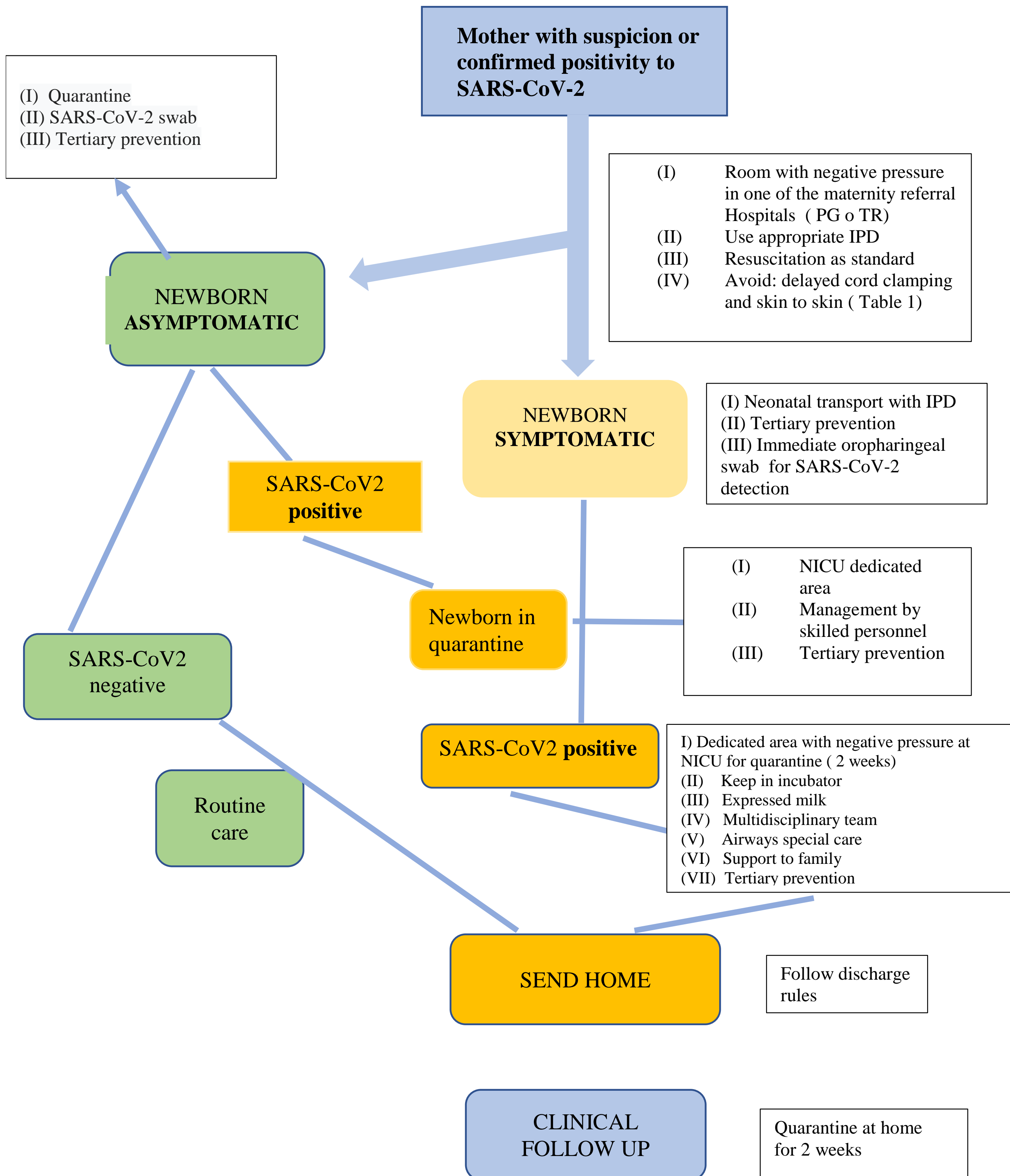

Figure 1 : Flow-chart for the perinatal-neonatal mangement of a suspicius or already confirmed positive mother to SARS-CoV-2

(Modified from *Wang et al.*. Ann Translat Med 2020)

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APPENDIX

Sampling and samples

UTM-VIRAL VAGINAL SWAB: should be carried out during labor and delivery by inserting the appropriate swab into the vagina deeply at the level of the posterior vaginal fornix. Send the sample to the reference laboratory of Microbiology and Virology

UTM-VIRAL RECTAL SWAB: should be carried out during labor and delivery by inserting the appropriate swab rectally. Send the sample to the reference laboratory of Microbiology and Virology

MATERNAL SERUM: should be collected at delivery from peripheral venous sampling. It will be transferred to a test tube (with acrylic gel). Invert the test tube 5-6 times and leave at room temperature for 30 min then centrifuge at 1500-2000 g for 10 min. Transfer the serum to another tube, with a screw cap. Freeze at - 80 ° (as an alternative to -20 °). Send the sample to the reference laboratory of Microbiology and Virology

UTM-VIRAL Oropharyngeal swab: should be carried out during labor. Send the sample to the reference laboratory of Microbiology and Virology

CORD BLOOD: should be collected at delivery after cleaning the cord with sterile gauze and saline solution to eliminate external blood. It will be transferred to a test tube (with acrylic gel). Invert the test tube 5-6 times and leave at room temperature for 30 min then centrifuge at 1500-2000 g for 10 min. Transfer the serum to another tube, with a screw cap. Freeze at - 80 ° (alternatively at - 20 °). Send the sample to the reference laboratory of Microbiology and Virology

UTM-VIRAL PLACENTAL SWAB: should be performed at delivery following a thorough cleansing of the fetal side with sterile gauze and saline solution: insert the swab, lift the fetal membrane and insert the swab obliquely for about 2 cm without exceeding the maternal side . Send the sample to the reference laboratory of Microbiology and Virology

PLACENTA BIOPSY: a placental biopsy from the fetal side (a cone with a base of about 3 cm including membranes) should be obtained, washed in sterile saline solution and inserted in a sterile container with screw cap . Freeze at - 80 ° (as an alternative to -20 °). Send the sample to the reference laboratory: Molecular Biology Laboratory, Dept of Obstetrics & Gynecology

HISTOLOGICAL PLACENTA EXAMINATION: should be performed on the remaining pathological samples following the aforementioned tissue biopsies. Methods of conservation and transfer of a positive COVID 19 placenta:
- if the structure has formalin, immerse the placenta + membranes + cord in the container with the fixative, seal tightly, insert the container in a plastic bag and the bag in a rigid tertiary container (as per regional provisions). Storage and dispatch at room temperature.
- if the structure does not have formalin, insert the placenta + membranes + cord in the vacuum bag and follow the procedures already established for closing the bag itself; then put the vacuum bag in a second plastic container and the latter in a third rigid container (as per

regional provisions). Storage and dispatch better if at controlled temperature (4-6 ° C, thermal bag with ice sticks). Placenta + membranes + cord, both in fixative and in vacuum, must be sent to the Pathology Lab.

OROPHARINGEAL NEWBORN SWAB: should be performed at birth. Send the sample to the reference laboratory of Microbiology and Virology

BREAST MILK: the first milk after colostrum should be collected sterile, store in a container with a screw cap. Freeze at - 80 ° (as an alternative to -20 °). Send the sample to the reference laboratory of Microbiology and Virology

The clinical advice provided above was developed under the auspices of the REGIONAL HOSPITALS NETWORK, UMBRIA, ITALY where there has recently been substantial experience of caring for patients with COVID-19 infection.

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