

**Appendix 1 – Major issues concerning SARS-CoV-2 in the neonate born from mother with SARS-CoV-2 infection**

<b>Delivery Room Management</b>		<b>Articles and guidelines</b>
<b>Umbilical cord clamping</b> (early <i>versus</i> delayed cord clamping)	Given a lack of evidence to the contrary, <b>delayed cord clamping is still recommended</b> , provided there are no other contraindications.	WHO guidelines <sup>1</sup> Obstetrician and Gynaecologists UK guidelines <sup>2</sup> Pregnancy and Labour Portuguese guidelines <sup>3</sup>
	The baby can be <b>cleaned</b> and <b>dried</b> as normal, while the cord is still intact.	Obstetrician and Gynaecologists UK guidelines <sup>2</sup>
	<b>Early umbilical cord clamping</b> is recommended with the aim of reducing the possibility of infection.	Neonatal Portuguese guidelines <sup>4</sup>
	If the mother has suspected SARS-CoV-2 infection and the isolation of both the mother and the newborn is adequate, late cord clamping <b>could be done</b> , although pros and cons should be analysed individually.	Neonatal Spanish guidelines <sup>5</sup>
<b>Skin-to-skin contact</b>	If the mother has suspected or confirmed SARS-CoV-2 and if the baby is well and does not require care in the neonatal unit, skin-to-skin contact can be done, although the pros and cons should be analysed individually. If the mother also requests skin-to-skin contact with her infant she should comply with strict preventive precautions.	Obstetrician and Gynaecologists UK guidelines <sup>2</sup> , Neonatal Spanish guidelines <sup>5</sup> , American neonatal guidelines <sup>6</sup>
	Skin-to-skin contact is <b>not recommended</b> .	Pregnancy and Labour and Neonatal Portuguese guidelines <sup>3,4</sup>
<b>Neonatal management</b>		
Guidelines are consensual in <b>implementing contact and droplet isolation measures</b> , limiting contacts and clinical and laboratory monitoring of newborns of SARS-CoV-2 suspected or infected mothers.		Neonatal Portuguese <sup>4</sup> , Spanish <sup>5</sup> , American neonatal guidelines <sup>6</sup> and UK guidelines <sup>7</sup>
<b>Breastfeeding</b>		
It is not yet clear whether SARS-CoV-2 can be transmitted via breast milk. Current guidelines recommend breastfeeding in asymptomatic or mild symptomatic infected mothers while ensuring contact and droplet isolation measures. Mechanical extraction of breast milk and administration to the newborn by a healthy caregiver can be an alternative, ensuring preventive isolation measures.		Neonatal Portuguese <sup>4</sup> , Neonatal Spanish <sup>5</sup> , American neonatal guidelines <sup>6</sup> , Pediatrics UK <sup>7</sup> and Italian <sup>8</sup> guidelines
<b>Treatment</b>		
Until now there is no specific treatment for neonatal SARS-CoV-2 infection. The main goal of treatment should be support measures. Inappropriate use of antibiotics should be avoided.		Neonatal Spanish <sup>5</sup> , Pediatrics UK <sup>7</sup> and Neonatal Portuguese <sup>4</sup> guidelines
<b>Antiviral drugs</b>	<b>Lopinavir/Ritonavir</b> is only recommended in neonates with $\geq 14$ days and after 42 weeks gestational age. Appropriate dosage in preterm infants and neonates $< 14$ days of age are not known and toxicity in premature infants can be severe. FDA strongly recommends that this drug should be avoided in this age group.	Pediatrics Portuguese guidelines <sup>9</sup> , Pediatrics Spanish guidelines <sup>10</sup> , FDA <sup>11</sup>

	Consider using <b>oseltamivir</b> until influenza virus infection is excluded.	Pediatrics Portuguese guidelines <sup>9</sup>
	Some guidelines suggest the use of <b>chloroquine and hydroxychloroquine</b> to treat SARS-CoV-2 infection in children but there is insufficient information about dosages and toxicity in the neonatal period.	Pediatrics Portuguese guidelines <sup>9</sup> , Pediatrics Spanish guidelines <sup>10</sup>
	Some guidelines suggest the use of <b>remdesivir</b> to treat SARS-CoV-2 infection in children, especially in critically ill patients with mechanical ventilation, but there is insufficient information about dosages and toxicity in the neonatal period.	Pediatrics Portuguese guidelines <sup>9</sup> , Pediatrics Spanish guidelines <sup>10</sup>
<b>Clinical signs in neonates born from mothers with SARS-CoV-2 infection</b>		
	No clinical symptoms (n = 9), prematurity (n = 4), low birthweight (n = 1) – total 9 newborns.	Chen HJ, <i>et al.</i> <sup>12</sup>
	Shortness of breath (n = 6), fever (n = 2), increased heart rate (n = 1), vomiting/ feeding intolerance (n = 1), refusing milk (n = 1) and gastric bleeding (n = 2), prematurity (n = 6), disseminated intravascular coagulation (n = 2), refractory shock, multiple organ failure and death (n = 1) – total 10 newborns.	Zhu H, <i>et al.</i> <sup>13</sup>
	Pneumonia (n = 3, all newborns with SARS-CoV-2 identified), lethargy and fever (n = 1 newborn with SARS-CoV-2 identified), lethargy, vomiting, and fever (n = 1 other newborn with SARS-CoV-2 identified), respiratory distress syndrome, shortness of breath, cyanosis and feeding intolerance (n = 1 the third newborn with SARS-CoV-2 identified) – total 33 newborns.	Zeng L, <i>et al.</i> <sup>14</sup>
	Feeding intolerance – total 1 newborn.	Wang S, <i>et al.</i> <sup>15</sup>
<b>SARS-CoV-2 PCR screening in neonates born from mothers with SARS-CoV-2 infection</b>		
	Samples collected from amniotic fluid, cord blood and neonatal throat swab were <b>negative</b> (n = 6) – total 9 newborns.	Chen HJ, <i>et al.</i> <sup>12</sup>
	All samples from neonatal throat swab were <b>negative</b> (n = 9) – total 10 newborns.	Zhu H, <i>et al.</i> <sup>13</sup>
	3 samples from nasopharyngeal and anal swabs were <b>positive</b> on days 2 and 4 – total 33 newborns.	Zeng L, <i>et al.</i> <sup>14</sup>
	<b>Positive</b> pharyngeal swab at 36 hours after birth. Negative cord blood, placenta and breastmilk specimens – 1 newborn.	Wang S, <i>et al.</i> <sup>15</sup>
<b>Other laboratory test findings in neonates</b>		
	Positive IgM antibodies to SARS-CoV-2 (2 hours after birth) – 1 newborn.	Dong L, <i>et al.</i> <sup>16</sup>
	Mild increase in myocardial enzymes (n = 1) – total 9 newborns.	Chen HJ, <i>et al.</i> <sup>12</sup>
	Thrombocytopenia complicated with abnormal liver function (n = 2) – total 10 newborns.	Zhu H, <i>et al.</i> <sup>13</sup>
	Leukocytosis, lymphocytopenia and elevated creatine kinase–MB fraction (n = 1), increased procalcitonin without other changes (n = 1), suspected sepsis, with an Enterobacter positive blood culture, leukocytosis, thrombocytopenia and coagulopathy (n = 1), normal laboratory test results (n = 30) – total 33 newborns.	Zeng L, <i>et al.</i> <sup>14</sup>
	Lymphopenia, increased aminotransferase, increased total bilirubin and elevated creatine kinase – total 1 newborn.	Wang S, <i>et al.</i> <sup>15</sup>
<b>Chest radiographic image</b>		
	Infections (n = 4), neonatal respiratory distress (n = 2), pneumothorax (n = 1), normal (n = 3) – total 10 newborns	Zhu H, <i>et al.</i> <sup>13</sup>
	Nonspecific findings (n = 30), pneumonia (n = 2), neonatal respiratory distress and pneumonia (n = 1) – total 33 newborns.	Zeng L, <i>et al.</i> <sup>14</sup>
	Thickened lung texture (n = 1) – total 1 newborn.	Wang S, <i>et al.</i> <sup>15</sup>

## REFERENCES

- 1- World Health Organization. Guideline: Delayed umbilical cord clamping for improved maternal and infant health and nutrition outcomes. Geneva: WHO; 2013.
- 2- Royal College of Obstetricians & Gynaecologists. Coronavirus (COVID-19) Infection in Pregnancy. London: RCOG; 2020.
- 3- Direção Geral da Saúde. Orientação nº 018/2020 de 30/03/2020. COVID-19: Fase de mitigação. Gravidez e parto. Lisboa: DGS; 2020.
- 4- Sociedade Portuguesa de Neonatologia. Recomendações para a abordagem do recém-nascido em contacto com a infeção por SARS-CoV-2 (COVID-19). Lisboa: SPN; 2020.
- 5- Sociedad Española de Neonatología. Recomendaciones para el manejo del recién nacido en relacion con la infeccion por SARSCoV-2. Versión 5.0. Fecha 23/03/2020. Madrid: Seneo; 2020.
- 6- Puopolo KM, Hudak ML, Kimberlin DW, Cummings J. Initial guidance: management of infants born to mothers with COVID-19. Itasca: American Academy of Pediatrics Committee on Fetus and Newborn, Section on Neonatal Perinatal Medicine, and Committee on Infectious Disease; 2020.
- 7- Royal College of Paediatrics and Child Health. COVID-19 guidance for paediatric services. London: RCPCH; 2020.
- 8- Davanzo R, Mosca F. Breastfeeding and SARS-CoV-2 infection. Milano: Società Italiana di Neonatologia; 2020.
- 9- Sociedade Portuguesa de Pediatria. Orientações para a abordagem e tratamento do doente pediátrico com COVID-19. Lisboa: SPP; 2020.
- 10- Asociacion Española de Pediatría. Documento de manejo clinico del paciente pediátrico com infeccion por SARS-CoV-2 -Extracto del Documento de Manejo Clínico del Ministerio de Sanidad. Actualización: 29 de marzo de 2020. Madrid: AEP; 2020.
- 11- Food and Drug Administration. USA: Prescribing information - Kaletra. Silver Spring FDA; 2016.
- 12- Chen HJ, Guo J, Wang C, Luo F, Yu XC, Xhang W, et al. Clinical characteristics and intrauterine cervical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet*. 2020;395:809-15.
- 13- Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr*. 2020;9:51-60.
- 14- Zeng L, Xia S, Yuan W, Yan K, Xiao F, Shao J, et al. Neonatal Early-Onset Infection with SARS-CoV-2 in 33 Neonates Born to Mothers With COVID-19 in Whuan, China. *JAMA Pediatr*. 2020 (in press). doi:10.1001/jamapediatrics.2020.0878.
- 15- Wang S, Guo L, Chen L, Liu W, Cao Y, Zhang J, et al. A case report of neonatal COVID-19 infection in China. *Clin Infect Dis*. 2020 (in press). doi:10.1093/cid/ciaa225.
- 16- Dong L, Tian J, He S, Zhu C, Wang J, Liu C, et al. Possible vertical transmission of SARS-CoV-2 from as infected mother to her newborn. *JAMA*. 2020 (in press). doi:10.1001/jama.2020.4621.