

# Review Article

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## Breastfeeding in COVID-19 Infection

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### Introduction:

In the beginning of 2020, the World Health Organization (WHO) announced a new strain of coronavirus, the SARS-CoV-2, which causes coronavirus disease 19 (COVID-19),<sup>1</sup> and led to the COVID-19 pandemic involving the whole world. In January 2021, only 1 year later, approximately 85 million cases had been confirmed, resulting in more than 1.8 million deaths.<sup>2,3</sup> Since then the total death toll was 52, 58,362 upto 4.12.2021.

During the same period, approximately 140 million births have been registered and a great dilemma arose regarding the possible need to discontinue the breastfeeding of infants of infected mothers.<sup>4</sup> Although, to date, evidence on the risk of vertical transmission, via the respiratory tract or through the breast milk itself, is limited, breastfeeding has generally been accepted as the preferred nutrition for the infant of the infected mother. In breast milk from infected mothers, IgA antibodies against SARS-CoV-2 have been detected, which may account for the reduced clinical impact of the disease in breastfed infants upon future viral exposure. Nonbreastfed had 14 times more risk of mortality than exclusively breastfed babies. Over 8,20,000 children's lives could be saved every year among children under 5 years, if all children 0-23 months were optimally breastfed.<sup>5</sup>

Before going to topic breastfeeding during Covid-19 infection, it would be better to recapitulate the benefits of breast feeding for child and mother.

### Benefits of Breastfeeding

Breastfeeding is the natural means of infant nutrition. Nature has designed the mother's breast milk to nurture the neonate and to protect the dyad in "psyche and soma", ensuring the proper growth and development in infant.

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Mother's milk is optimally suited for her infant. Breastfeeding enhances both maternal and infant health, with a dynamic, bidirectional exchange between the mother and the infant.<sup>1</sup> It also favors the bond between mother and child, provides higher IQ, and greater professional success in the future.<sup>6-8</sup> Regarding immunological protection, its effect is particularly important against infectious diseases that benefit from the direct transfer of antibodies and other anti-infectious factors, favoring also the lasting transfer of immunologic competence and memory.<sup>6,8</sup>

The multiple bioactive components have been identified in breast milk that not only protect against infections but improve neurocognitive and immunologic development of the child since Lars A Hanson first described secretory Immunoglobulin A (sIgA) in breastmilk in 1961.<sup>9-11</sup>

Skin-to-skin contact and kangaroo mother care facilitate breastfeeding as well as improve thermoregulation, blood glucose control, and maternal-infant attachment, and decrease the risk in mortality and severe infection among low birth weight infants.<sup>12,13</sup> Beyond the neonatal period, positive effects of mother-infant holding include improved sleep patterns, lower rates of behavioural problems in the child and higher quality parental interaction.<sup>14,15</sup> The absence of breastfeeding and the interruption of exclusive breastfeeding in the first six months led to, the loss of 341.3 billion dollars annually due to diseases and death of children and maternal death due to diabetes and Cancer.<sup>16</sup>

### Benefits for Infant:

Breastfeeding protects against morbidity and mortality in the neonatal and post-periods, as throughout childhood. It protects infant, children and also adult from different diseases and condition.<sup>17</sup>

**Infectious diseases:** Breastmilk is protective and associated with a 64% reduction in the incidence of non-specific gastrointestinal infection, reduction of any type of infectious disease including respiratory infection and others.

**Sudden Infant death syndrome (SIDS):** In breastfed babies the incidence of SIDS much lower than the formula fed babies. Breastmilk reduces SIDS by approximately by 50% throughout all ages of infancy.<sup>18</sup>

**Necrotizing enterocolitis:** Breastmilk is associated with 58% to 79% reduction in the incidence of development of necrotizing enterocolitis.<sup>17</sup>

**Allergies, Asthma, Rhinitis, Eczema:** A Finnish study showed Breastfeeding is associated with 27% -42% reduction in risk of development of allergic and atopic diseases.<sup>17</sup>

**Celiac disease:** There is 52% reduction in the risk of development of Celiac disease in infants with BF at the time of introduction of gluten. Breastfeeding facilitates growth of Lactobacillus Bifidus which in turn helps intestinal wall not to become inflamed.<sup>19</sup>

**Hypertension, Obesity, Cardiovascular risk and Diabetes:** A prospective British study showed that those preterm babies who were breastfed had significantly lower mean and diastolic blood pressure.<sup>20</sup> There was also 15-30% reduction of risk for obesity among those in adulthood. Reduction of LDL 7mg/dl and 33% less risk of developing diabetes were also reported among breast fed babies.<sup>17</sup>

**Malignancies:** Breastfeeding for 6 months or more was associated with 19% reduction of risk of developing leukaemia in childhood. It was also reported as inversely associated with neuroblastoma.<sup>21,22</sup>

**Peptic ulcer diseases:** A systemic review found that Breastfeeding is protective against Helicobacter pylori infection in child and adulthood.<sup>23</sup>

**Neurodevelopment:** A meta-analysis reported that intelligence quotient was 3.44 points and cognitive development was also 3.16 points more in breastfed as compared to formula-fed. Breastfeeding more than 6 months also reduces risk of development of attention deficit disorder and Autistic spectrum disorder.<sup>24</sup>

**Breast milk for preterm babies:** Milk from woman who delivered prematurely is higher in protein, fat, free amino acids and sodium, and full of bioactive, immunological and growth factors. So, this milk is especially suited for her baby resulting in improved survival and better neurological developments.<sup>25</sup>

#### **Benefits of Mothers:**

Breastfeeding (BF) seems to be related to good physical and emotional health for the mother during

the puerperium, the lactation period and all her future life.<sup>26</sup> Epidemiological studies have demonstrated that, compared with women who did not breastfeed, lactating women reported seeking for medical care less often, a lower frequency of respiratory, cardiovascular and gastrointestinal diseases, as well as fewer symptoms related to emotional problems.<sup>27,28</sup>

There are some immediate and long-term benefits of breastfeeding for mother's health .

The immediate benefits are: uterine involution , reduced bleeding and infection, lactational amenorrhea, reduced adiposity and weight, postpartum depression, stress and anxiety and improved body image.<sup>26</sup>

The long-term benefits are: Reduced cancer (breast, ovarian, endometrium), endometriosis, diabetes, osteoporosis, blood pressure and cardiovascular diseases, metabolic syndrome, rheumatoid arthritis, Alzheimer disease and multiple sclerosis.<sup>26</sup>

#### **Uterine involution and reduced bleeding**

Early suckling is one of the most important stimuli for the production of oxytocin, which is responsible for uterine contraction, accelerating the return of the organ to its normal size and reducing the occurrence of postpartum hemorrhage and anemia.<sup>29</sup>

#### **Lactational amenorrhea**

During the lactation period, both progesterone and estrogen are suppressed, with the occurrence of a period of amenorrhea and infertility.<sup>30</sup>

#### **Weight and body image**

During breastfeeding, there are more rapid weight loss and the return to pre-gestational conditions, with an average monthly reduction of 450 g in the maternal weight.<sup>26</sup>

#### **Postpartum depression**

It is known that 13% of all puerperal mothers may develop signs and symptoms of depression within a period of 12 weeks after delivery.<sup>18</sup> Breastfeeding causes decrease the postpartum depression.<sup>26</sup>

Breast cancer, ovarian cancer, cancers of the endometrium

It is estimated that the risk of breast cancer can be reduced by more than 4% each year of BF.<sup>31</sup> A 16% increase in the proportion of mothers who breastfeed for 6 months can reduce the expected prevalence of breast cancer by 1.6% per year. The relative risk of developing ovarian cancer is estimated to be reduced

by 2% for each month of BF.<sup>32</sup> Long periods of BF are also associated with a reduced risk of endometrial cancer.<sup>33</sup>

### **Endometriosis**

For every additional 3 months of total BF per pregnancy, women experienced an 8% lower risk of endometriosis.<sup>34</sup>

### **Diabetes**

Meta-analysis studies have detected a statistically significant inverse association between BF duration and risk of type 2 diabetes.<sup>35</sup> And with a reduction of 4–12% of the risk of developing type 2 diabetes with each additional year of lactation.

### **Osteoporosis**

Breastfeeding can contribute to the reduction of the risk of osteoporosis in future life since it has been demonstrated that lactating women have a bone mass with higher mineral density.<sup>36</sup>

### **Blood pressure**

Studies correlating BF with blood pressure have detected lower levels of both systolic and diastolic pressure among nursing mothers during the BF period, with the observation of a long-lasting dose–response effect, even though this effect may not persist until old age.<sup>37</sup>

### **Cardiovascular diseases**

Women who breastfeed for long periods of time, 7–12 months after the first delivery, have a 28% lower risk to develop vascular diseases compared with women who never breastfed.<sup>37</sup>

### **Metabolic syndrome**

Metabolic syndrome (MS) is the result of several changes that include central obesity, arterial hypertension, dyslipidemia and insulin resistance, which when associated, involve severe complications and high mortality rates. It is known that women who breastfeed for prolonged periods have a lower risk of the incidence of MS, a 12% reduction in the risk of MS development has been observed for each year of lactation.<sup>38</sup>

### **Rheumatoid arthritis**

A recent meta-analysis by Chen et al.<sup>39</sup> demonstrated that BF is associated with a lower risk of rheumatoid arthritis among nursing women, whether or not the duration of BF is longer than 12 months.

### **Alzheimer disease**

Fox et al.<sup>40</sup> studied a cohort of elderly English women and observed that the risk of developing Alzheimer disease was lower among those who had breastfed, possibly owing to the hormonal effects of estrogens on brain receptors and of insulin sensitivity triggered by breastfeeding.

### **The Anti-Inflammatory Effects of Breastfeeding: Knowledge Gained From Other Respiratory Viruses**

Respiratory infections are a leading cause of morbidity in children. During the first year of life, breastfeeding provides protection from these infections, which is dependent on its duration.<sup>41</sup> The immaturity of the infant's immune system at birth increases the risk of infection by external agents, including viruses and bacteria.<sup>42</sup>

Breast milk changes in synthesis, from colostrum through a transitional stage to mature milk, ensuring appropriate nutrition for the infant.<sup>43</sup> Regarding immunity, human milk induces in the infant the regulation and development of the innate and adaptive immune systems.<sup>44</sup> with a major long-term role in health and disease.<sup>45</sup> The anti-inflammatory protection conveyed by breast milk is effected by both chemical components and cellular interactions. Colostrum and transitional milk safeguard the infant via an abundant glycoprotein, lactoferrin, which has multilevel actions, lympho-stimulatory, anti-inflammatory, anti-bacterial, anti-viral and anti-fungal.<sup>46</sup> Its protective functions are attributed to its iron-binding properties, inhibition of interleukin-1b (IL-1b) and tumor necrosis factor-alpha (TNF-a), stimulation of the activity and maturation of lymphocytes, and preservation of an antioxidant environment. Lactoferrin, along with other milk peptides protects against bacteria and fungus.<sup>47</sup> Milk regurgitation into the nose after breastfeeding has been suggested to increase phage adherence to mucosal surfaces in the respiratory tract, in addition to the gut, eliminating in this way mucosal bacteria and protecting against recurrent respiratory infections in breastfed infants, in the longer term.<sup>48</sup>

New knowledge gained during the 2003 SARS-CoV-1 epidemic was that lactoferrin interacts with heparin sulphate glycosaminoglycan (HSPG) cell receptors, interfering with the first anchoring sites of the virus on the cell, and thus preventing the initial contact between the SARS-CoV and host cells. Lactoferrin has also been shown to block the interaction between spike viral protein and HSPC in an angiotensin converting

enzyme 2 (ACE2) receptor, which otherwise results in the full infection.<sup>49</sup>

Breast milk contains cells with stem/progenitor properties and has the capabilities to differentiate into neuronal lineage. Human breast milk is rich in miRNA and so far 386 different miRNA were identified in breast milk and are involved in regulation in T and B cells development, release of inflammatory mediators and epigenetic regulation of stem cells. The epigenetic role of breast milk in preventing infectious diseases and disorder immune phenotype may be linked to the expression of regulation of pro-inflammatory cytokine gene.<sup>50</sup>

Oligosaccharides in human milk serve both as a direct barrier to pathogens and as a prebiotic, i.e., aliment for probiotics, which promote synthesis of a healthy microbiota.<sup>42</sup> The binding capacity of the oligosaccharides has proven protective against viruses with high morbidity and mortality.<sup>51</sup> Additional protective properties of breast milk are provided by the transfer of maternal immune cells to the infant, including macrophages, neutrophils and lymphocytes.<sup>52</sup> The concentration of these cells in the human breast milk vary according to the age of the infant. Thus, the proportion of the different leukocytes vary between colostrum (macrophages 40–50%, neutrophils 40–50% and lymphocytes 5–10%) and more mature milk (macrophages 85%, lymphocytes 15%).<sup>53</sup>

The immune properties of the mother are also transferred to the breastfed infant in the form of secretory IgG<sup>54</sup> and IgA in maternal milk. Breast milk attains the highest concentration in IgG antibodies in the colostrum, and their concentration drops after the first month of life.<sup>55</sup> IgG antibodies, transferred to the fetus through the placenta during intrauterine life and to the infant after birth in breast milk, constitute the infant's first defense system. In mothers immunized against RSV, s-IgG antibodies were detected in breastmilk, providing protection to the infant against the main cause of respiratory infection during the first year of life. IgA antibodies coat the GI and respiratory mucosa and block the entrance of foreign antigens<sup>46</sup> and viruses. In premature infants, the IgA levels are higher, for enhanced protection.<sup>56</sup> In the event of an infection, in either the mother or the child, breast milk conveys a plethora of anti-pathogenic and anti-inflammatory bioactive factors to protect the infant.<sup>57</sup>

Breastfeeding has been documented to exert more effective protection against a spectrum of pneumonia-causing viruses, including influenza, RSV and parainfluenza, in girls than in boys;<sup>58</sup> these findings were interpreted by the researchers as a “nature”-provided advantage for survival of females, in order to preserve the species. Protection against viral invasion appears to be enhanced by the regurgitation of breast milk into the upper respiratory tract, conveying viable commensal, mutualistic, and probiotic bacteria and viruses that colonize the upper respiratory tract, contributing to the maturation of the infant's immune system.<sup>48,59</sup> Bacteria in the human milk are one of the earliest sources of prokaryotic microorganisms transferred to the infant, following the maternal microbial colonization through the amniotic fluid, placenta and umbilical fluid<sup>60</sup> and a more substantial transmission of vaginal and gut microorganisms to the newborn through the birthing canal.<sup>61</sup> The human milk microbiota (HMM) originates from the maternal GI tract and skin, and from the infant's mouth which enhance the maturation of both innate and adaptive immune systems.<sup>62</sup>

#### **Benefits of Breastfeeding for Covid19:**

In children, COVID-19 infection rates are lower than in adults, while fatality rates are almost zero.<sup>41</sup> Children generally have milder symptoms, but there are reports of the development of a novel multisystem inflammatory syndrome in children (MIS-C, somewhat similar to Kawasaki disease, predating continuous vigilance.<sup>61</sup> International and national health authorities strongly recommend exclusive breastfeeding for at least the first six months of life: “Breastfeeding is one of the most effective ways to ensure child health and survival”(WHO)<sup>3</sup>; “Low rates and early cessation of breastfeeding have important adverse health and social implications for women, children, the community and the environment, result in greater expenditure on national health care provision, and increase inequalities in health” –(European Commission).<sup>62,63</sup> It is a mainstay for promoting the immune development of the infant by both immunological factors transferred from mother to infant through breast milk and microorganisms colonizing the organs.<sup>64</sup>

SARS-CoV-2 is probably transmitted in multiple ways, including through droplets via the respiratory tract and invasion by enterocytes.<sup>61</sup> GI symptoms manifest first in infancy, and lactoferrin in breast milk has been suggested to be capable of strengthening junctions

between microbes in the gut and thus amplifying the innate defense. Although at present, this is only an assumption for SARS-CoV-2, in other strains of SARSCoV, lactoferrin was shown to increase mucosal immunity and prevent viral anchoring on cell receptors.<sup>65</sup> Cytokines and growth factors in breast milk excite the infant's immune system and balance the anti-inflammatory and pro-inflammatory cytokines, lessening their effect and preventing the "cytokine storm" described in other viral infections, such as H1N1 swine flu and H5N1 bird flu.<sup>66</sup>

The most abundant antibody in breast milk, s IgA, provides adequate specific protection against pathogens, among which also are viruses. The specificity of s IgA is determined by the immune response of the mother to previous infection, probably explaining the low rates of infection or milder symptoms of the infected breastfed infants of SARS-CoV-infected mothers. The evidence to date on pregnant women infected by SARS-CoV-2 does not demonstrate a more severe or complex clinical picture than in the general infected population. In view of the time-dependent protective effect of exclusive breastfeeding against viral infections, and the increased maternal contact of the breastfed infant compared with the infant receiving artificial or mixed and the high transmissibility of SARS-CoV, protective measures should be strictly observed for safeguarding the lactation process.<sup>41</sup>

### **Breastfeeding recommendations in different Covid-19 situation**

#### **SARS-CoV-2-Positive Mother Before or on Delivery**

Some mothers were prohibited from holding the neonates, in order to minimize the risk of infection<sup>67,68</sup> and expressed breast milk was proposed as the optimum feeding solution.<sup>69</sup> Mothers in a good clinical condition were encouraged to breastfeed, with all appropriate instructions and precautions.<sup>70</sup> In the case of admission of preterm infants to the neonatal intensive care unit (NICU), expressed breast milk was suggested, if available.<sup>67</sup> Overall, among the 231 births from SARS-CoV-2-positive mothers, 13 neonates (5.8%) tested positive within the first 48 hours of life.<sup>71</sup>

**SARS-CoV-2-Positive Lactating Mother, With Negative Infant** Generally, breastfeeding was encouraged<sup>72-74</sup> but in order to reduce the risk of infection<sup>67</sup> instructions for appropriate precautions were given. Measures undertaken to minimize the risk

of transmission during breastfeeding were mask wearing, handwashing, routine cleaning and disinfection of all surfaces touched, thorough cleaning and sterilization of infant feeding equipment before and after use, breast washing with gauze saturated with soap and water, and avoidance of falling asleep with the baby with, expression of breast milk and feeding of the infant by a healthy family member or a caretaker was recommended.<sup>72</sup> Of a total of 63 women, 37 (58.7%) discontinued breastfeeding and were isolated from their babies. Of over 38 samples of breast milk tested in SARS-CoV-2-positive mothers, only 2 (5.2%) were positive for SARS-CoV-2.<sup>74</sup>

#### **Both Mother and Infant SARS-CoV-2-Positive**

Breastfeeding was strongly encouraged where both members of the dyad were positive<sup>75</sup> and further investigation was suggested on the role of IgG antibodies in the possible protective role of breast milk antibodies on the immunity of the infants.<sup>75</sup> Among the breast milk samples tested for SARSCoV-2, 27% (3/11) were positive but the milk was not considered to be the cause of infection of the infants.<sup>76</sup>

#### **Healthy mother and Infant SARS-CoV-2-Positive**

In reported cases healthy mother remained with infected infants and continued breastfeeding. It is found that despite the closed contact mothers remained Covid negative.<sup>1</sup>

#### **Effect of separation of mother and baby**

Negative effect of separation of mothers and infants causes increased maternal stress leading decreased breast milk, loss of innate and adaptive immunity of the infant. In infant there is also increased stress, loss of skin-to-skin care benefits leading to increased instability, hypoglycemia and increased need of intensive care. After all there is increased stress in family. Ultimately there is reduced breastfeeding success.<sup>77</sup>

The evidence suggests that health management services must consider the deleterious impact when implementing policies and guidelines.<sup>78</sup> Adding to previous knowledge about the impact of separation of mothers and infants and considering the psychological impact of COVID-19 and related restrictions (including separation) on mothers' mental health, psychological interventions should be incorporated in health-care protocols.<sup>79</sup> In fact, current guidelines formulated specifically to address the postpartum period during the COVID-19 pandemic strongly recommend the

maintenance of breastfeeding practices.<sup>80</sup> Specifically, health services should rethink how they provide this support during the pandemic, namely, through tele-health and in-person when possible. Communication of evidence-based information and access to technical assistance and support should be provided for all families.<sup>81</sup>

### **Vaccination of mother with SARS-CoV-2 and Breast milk**

In pregnant women vaccinated with mRNA vaccine, vaccine elicited antibodies were transported to infant by cord blood and breast milk.<sup>82</sup> All antibodies against SARS-CoV-2 are found in breastmilk after vaccination which may neutralize the virus.<sup>83</sup>

Key messages and priorities set by UNICEF and Global Nutrition Cluster<sup>84</sup>

1. Programs and services to protect, promote and support optimal breastfeeding (early and exclusive) and age-appropriate and safe complementary foods and feeding practices should remain a critical component of the programming and response for young children in the context of COVID-19.
2. Mothers with suspected or confirmed COVID-19 and isolated at home should be advised to continue recommended feeding practices<sup>1</sup> with necessary hygiene precautions during feeding.
3. Alignment and coordination in the mitigation plans across nutrition, health, food security and livelihood, agriculture, WASH, social protection and mental health and psychosocial support to focus on reaching infants and young children in the context of COVID-19.
4. Actions through relevant systems (Food, Health, WASH, and Social Protection) should prioritize the delivery of preventive services to mitigate the impact of the pandemic on young children's diets and wellbeing with strong linkages to early detection and treatment of child wasting.
5. Full adherence to the International Code of Marketing of Breast-milk Substitutes and subsequent WHA resolutions (including WHA 69.9 and the associated WHO Guidance on ending the inappropriate promotion of foods for infants and young children) in all contexts in line with the recommendations of IFE Operational Guidance.

6. Donations, marketing and promotions of unhealthy foods – high in saturated fats, free sugar and/or salt – should not be sought or accepted.
7. Mothers with suspected or confirmed COVID-19 and isolated at home should be advised to follow necessary respiratory hygiene during feeding
8. Intensify support to families on what, when and how to feed young children at home during the complementary feeding period using practical communication platforms to reach families in the context of COVID-19.
10. Intensify promotion of safe hygiene behaviours especially hand washing with soap at all critical times and practicing safe food preparation/handling to reduce risk of transmission of COVID-19.
11. Make simple, practical and context-specific information available using all available communication channels (digital, broadcast and social media) to the families on healthy feeding options for young children in the context of lockdowns and financial barriers.

### **Recommendation:**

Despite concerns of transmission from the infected mother to the infant, global and national health stakeholders have so far univocally encouraged breastfeeding during the COVID-19 pandemic. The WHO, the United Nations International Children's Emergency Fund (UNICEF), the Union of European Neonatal & Perinatal Societies (UENPS), and the US Centers for Disease Control and Prevention (CDC), all highlight the well-established overall short and long-term immunological and psychosomatic benefits of breastfeeding for the dyad. For this reason, strict measures of mother-infant separation and discontinuation of breastfeeding are to be avoided, regardless of a positive diagnosis and the intensity of symptoms, unless the severity is of such a level that the mother cannot take care of the infant, in which case, expressed, fresh, unpasteurized breast milk should be provided for the baby.

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