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Understanding the Impact of Maternal Health on Neonatal Disease: A New Horizon

Critically ill neonates, whether premature or those born closer to full-term gestation, can have adverse outcomes following untimely exposure to many physiological and other potentially pathogenic stimuli *in utero* and after birth.[1–3] In many organ systems, even minor alterations in the course of maturation can cause abnormalities.[4,5] Carefully designed studies are needed to extrapolate the experience from one part of the world to another;[6,7] there are important genetic, infectious, and cultural differences that might affect outcomes. However, in many situations, there are vertical influences where information about maternal health can help us in understanding neonatal disease and in predicting its outcomes.[8]

We have long believed that the fetus grows in a sterile uterovaginal tract.[9] However, recent studies have identified bacterial flora in the birth canal.[10] The impact of this colonization on a fetus developing *in utero* is still unclear, but there is a possibility that the presence of these bacteria on mucosal surfaces might alter perinatal outcomes.[11] The effect on the developing fetal immune system also needs study, particularly with emerging information about many subclinical infections prevalent in many parts of the world.[12,13] There is a need for improved understanding of the impact of these infections on the developing immune system.

In addition to the bacterial flora, nutrition is another important stimulant for the rapidly growing organs, be it the central nervous system, immunity, or the endocrine system.[14] The nutritional experiences of the newborn infants may have lifelong effects.[15] Human milk contains fats in high concentrations, which seem to be important as a source of energy and in maturation of the neurological and mucosal immune systems.[16,17] Milk fat content and composition are highly dynamic parameters in early infancy, and need careful analysis.[18] However, despite increasing awareness about the importance of human milk, we also now know about the factors that may curtail its availability. Mothers of infants who are critically ill experience a high degree of anxiety, and may not always able to provide milk for their infants.[19,20] The availability of human milk may also be limited in situations such as maternal illness, ongoing drug therapy, or substance abuse.[21] In these situations, human milk banks can be an important resource but there are many restrictions—natural and human-created.[22]

We have been able to make important progress in the treatment of many life-threatening neonatal illnesses.[23] These advances have not only reduced neonatal deaths, but have also facilitated major societal changes; fewer neonatal deaths have helped in reducing the total number of pregnancies per woman as she is reassured about the number of surviving infants. Fewer pregnancies have helped reduce maternal mortality.[24,25]

In the *Newborn*, we aim to cover problems that a baby might develop *in utero*, the perinatal period, following birth, and the implications of these abnormalities during the first 1000 days after birth. In this 4th issue of the first volume, we present 8 important articles (**Fig. 1**). There are 3 important papers focused on the impact of infectious agents on the developing immunity. Padhi *et al*.[26] have examined the prevalence of gram-negative bacteria in maternal cervical secretions. They are investigating early-onset sepsis (EOS) seen within 72 hours following birth.[2,27] These infants likely acquire the bacterial pathogens from the maternal cervical/vaginal secretions during the perinatal period.[27–29] In the West, EOS is caused most frequently by gram-positive bacteria such as group B Streptococci (GBS), *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus viridans*, and *Enterococcus* spp. Gram-negative pathogens are seen in some cases.[27,30–33] However, in tropical and peri-equatorial regions, EOS may be caused more frequently due to gram-negative pathogens.[34–38]These authors evaluated the literature for the quality of data, and performed a systematic review and meta-analysis of 15 studies. They show that gram-negative colonization of the maternal cervical-vaginal tract in tropical/peri-equatorial regions of the world was more frequent than previously recognized. Early identification of these pathogens may help in timely evaluation and treatment of these infants.

In another study, Anand *et al*.[39] reviewed congenital/perinatal hepatitis B infections in neonates. Hepatitis B infections are estimated to affect more than 2 billion people worldwide. The overall prevalence of HBsAg positivity in plasma may be only 3.5%, but it varies depending upon the geographic area. In exposed infants, universal hepatitis B vaccination and the administration of hepatitis B

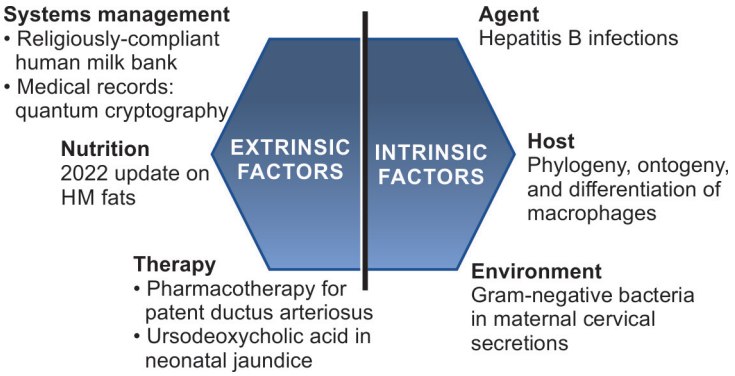

Fig. 1: **Areas of focus in the *Newborn*, volume 1, issue 4.** The *newborn* has expanded the traditional agent-host-environment trinodal disease model to a hexagonal system. The three additional foci represent extrinsic factors that can affect health; these originate in therapy, nutrition, and systems management.

immunoglobulin (HBIg) within 12 hours following birth can reduce the risk of perinatal infection.[40] Knowing the importance of these fetal/neonatal infections, we also needed to study the host defense mechanisms. Unlike in adults, macrophages are the major resource for innate cellular immunity in neonates.[41] In terms of the numerical content, the largest macrophage population is in the gastrointestinal tract.[42] An article has been devoted to track the ontogeny, phylogeny, and the development of intestinal macrophages.[43]

In a survey of the readership of the *Newborn*, we noted that the readers sought a comprehensive review of fats in human milk. The fat content of human milk is high, and hence, these constitute an important set of nutrients for newborn infants. Fats are also needed for neurological development in newborn infants. Many readers suggested that the Global Newborn Society needs to assume responsibility here and regularly provide information on milk fats. Hence, this article has been named as providing the 2022 updates on chemical composition of human milk.[44]

This issue contains a very important article that traces the development of a religiously compliant human milk bank (HMB) in Bangladesh. Rahman et al.[45] have made major efforts to develop and maintain this facility. HMBs similar to those in the West have been difficult to establish in Muslim countries as the Islamic law does not allow consumption of unidentified donated milk from multiple donors. Human milk is known to be important for nutrition in premature and critically ill infants, and so there is a need to develop religiously compliant and conditionally identified HMBs in Muslim countries. In these milk banks, every mother's milk is processed and stored separately, and the milk provided by one mother can be provided to an infant from a different family only after appropriately counseling both families about the Islamic law of prohibition of future marriages between milk siblings. Documents related to these issues are provided to both families and data need to be maintained for future reference.

There are two important papers on evaluation of the quality of evidence for treatment modalities in neonatal intensive care units. Arif et al.[46] performed a systematic review to evaluate the effect of ursodeoxycholic acid in unconjugated hyperbilirubinemia in term neonates treated with phototherapy. The combination of these two treatments reduces the bilirubin levels and duration of phototherapy, although there is a need for further treatment. In another article, Srivastava et al.[47] evaluated pharmacologic therapy for patent ductus arteriosus closure[7] in preterm small-for-gestational-age infants. They observed a similar rate of PDA closure following the first course of non-steroidal anti-inflammatory drug (NSAID) therapy between appropriately grown and growth-restricted neonates. However, severe growth restriction[48] (birth weight Z-score[49] below –2) was associated with higher rates of PDA ligation as compared to normally grown infants.

Finally, we have a review article describing the possibility of using quantum cryptography for securing personal health information in hospitals.[50] In our healthcare systems, we have been able to efficiently store healthcare information, retrieve it in a timely fashion, and ensure its safety.[51] However, the data are increasing rapidly and our current computational systems could well become inadequate in the not-so-distant future.[52] This article reviews the possibility of using quantum computing algorithms/devices that can provide elegant solutions based on subatomic interactions.[53,54]

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