Norovirus study shows how bile acids in breast milk affect newborn gut health

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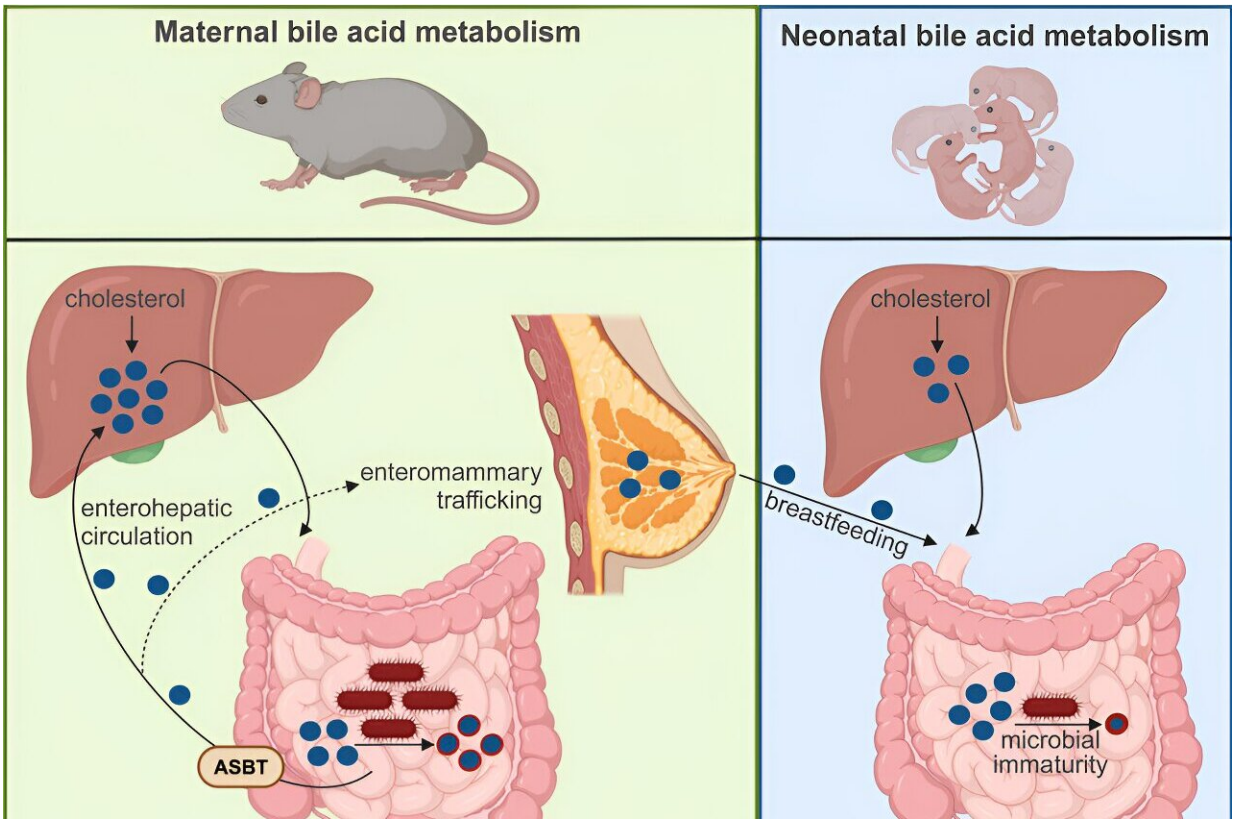

Graphical abstract. Credit: *Cell Host & Microbe* (2024). DOI: 10.1016/j.chom.2024.08.003

A University of Florida researcher has compiled the first-ever study that identifies the role of breast milk bile acids—a breakthrough that could

help lessen the incidence of the deadly norovirus in infants, which claims the lives of at least 50,000 children every year.

Because newborns don't have an established gut microbiome—the collection of friendly bacteria that helps humans digest nutrients and respond to intestinal pathogens—they are especially susceptible to the norovirus, which is one of the leading causes of newborn deaths worldwide.

"We knew microbiota protected adult mice from norovirus infection and we knew newborns were vulnerable to severe norovirus disease," said Stephanie Karst, Ph.D., a member of the UF Emerging Pathogens Institute and a professor in the UF College of Medicine, who led a recent mouse-model study on norovirus that was published on Aug. 29 in *Cell Host & Microbe*. "So, that led us to ask the question: Are newborns vulnerable to norovirus because their gut microbiota is immature?"

The liver produces cholesterol, which is then converted into bile acids —metabolites that get secreted into the intestine to help digest fat during eating. In the gut, certain microbiota then convert these bile acid metabolites into microbial bile acids, which can protect against norovirus infection. However, newborns lack the proper gut bacteria to produce these protective microbial bile acids, leaving them unprotected from norovirus disease.

But the story doesn't end there. While microbial bile acids play a protective role during norovirus infection, host bile acids actually promote infection. Newborns have high levels of these host bile acids, not only because they aren't modified by gut bacteria, but also because they are found in breast milk.

According to Karst, "The severity of norovirus infection is determined by the balance between host bile acids that enhance infection and

microbial bile acids that inhibit it."

Because newborns do not have the right gut microbes to modify bile acids and they ingest host bile acids in breast milk, they are left only with the metabolites that make them susceptible to more severe norovirus infections.

While noroviruses take advantage of this fragile metabolic environment in newborns, breastfeeding protects the baby in many other ways and milk bile acids likely have positive effects as well. In fact, Karst and colleagues found that the acids protect the baby from intestinal injury outside of the context of virus infection.

With more research on the maternal and newborn bile acid landscape, Karst hopes the findings will inform future efforts to treat newborn norovirus.

"The yin and yang—exacerbating norovirus infection but protecting from other intestinal insults—really highlights that we need to have a comprehensive understanding," Karst said. "Because we don't want to manipulate the breast milk bile acid pool and leave the baby exposed to other types of intestinal injuries."

Norovirus is not the only virus influenced by metabolites like bile acids. Influenza, chikungunya, and herpes viruses, for example, are inhibited by the same types of microbial bile acids that are not present in newborns. Meanwhile, host bile acids also promote human coronavirus infection.

"Additionally, there are many other metabolites that are being delivered to babies in breast milk," Karst said. "I think this will, hopefully, open up other arms of research looking at metabolite interactions with pathogens and how they influence newborn susceptibility."

More information: Amy M. Peiper et al, Metabolic immaturity and breastmilk bile acid metabolites are central determinants of heightened newborn vulnerability to norovirus diarrhea, *Cell Host & Microbe* (2024). DOI: 10.1016/j.chom.2024.08.003