With Milk Composition, Infant Gut Microbiome, and Growth Human Cytomegalovirus in Breast Milk is Associated

Researchers investigate the effects of human cytomegalovirus (CMV) reactivation on breast milk composition.

Study

In the present study, researchers explore the influence of CMV reactivation in mammary glands during lactation on the composition of human breast milk. To this end, data from the Mothers and Infants LinKed for Healthy Growth (MILK) project were utilized, which included milk samples obtained during a study visit one month postpartum through full breast milk expression two hours following a complete infant meal. The metabolome and any differences in the composition of human milk samples were also assessed.

The relationships between metagenomic principal components (PCs) that explained at least 5% of the data variation and milk CMV status were evaluated. Differentially expressed genes were also identified based on the quantity of newborn fecal microbial taxons, measured infant development, and compared it to milk cytomegalovirus status. Structural equation modeling (SEM) was used to investigate the relationship between milk CMV, kynurenine, and newborn development.

Multi-omics data from mother-infant dyads were used to determine the distribution of CMV-mapped deoxyribonucleic acid (DNA) reads in milk samples with at least one read mapped to the CMV genome. Anthropometric data were also used to identify disparities in newborn development linked with milk CMV reactivation.

Shotgun DNA sequencing data from postpartum milk samples was performed to identify samples with CMV viral shedding. CMV-positive samples had at least one read mapped to the CMV genome, whereas CMV-negative samples did not. Quantitative polymerase chain reaction (qPCR) analysis was used to identify CMV DNA in 187 samples and validate the approach.

Single-cell ribonucleic acid (RNA)-sequencing data from human milk was utilized to investigate the expression patterns of 36 differentially expressed genes across milk cell types. Linear regression models considered study location, parity, mother age, pre-pregnancy body mass index (BMI), maternal self-identified race, gestational diabetes status, and maternal Healthy Eating Index (HEI) score as factors to evaluate differences in the abundance of 458 metabolites between

58 and 84 CMV-positive and negative milk samples, respectively. The association between milk CMV status and the infant gut microbiome composition was also assessed.

Results

Shotgun sequencing and qPCR results were similar, with the shotgun sequencing approach having 93% sensitivity and 95% specificity for identifying CMV-positive samples and 88% sensitivity and 97% specificity for CMV detection.

Increased expression of immune response genes was observed in CMV-positive milk samples. CMV-positive milk samples were also associated with higher amounts of basic-type leucine zipper transcription factor 2 (BATF2) and indoleamine 2,3-dioxygenase 1 (IDO1) genes. Differentially abundant metabolites in CMV-positive samples revealed increased activation of the IDO tryptophan to the kynurenine metabolic pathway.

Milk CMV status was related to the newborn gut microbiome, with decreased amounts of Bifidobacterium present in the gastrointestinal tract. However, milk CMV status was unrelated to newborn fecal alpha diversity.

Infants provided CMV-positive milk exhibited an average weight-for-length advantage of one-third of Z-scores compared to those consuming CMV-negative milk at one month. This association between WLZ values and one-month milk CMV status was not observed at delivery or after six months.

Infants consuming CMV-positive milk exhibited lower average length-for-age Z scores and no change in weight-for-age Z scores at one month. A negative association was observed between the fraction of CMV-mapped readings in milk and newborn WLZ at one month but not six months.

Even after controlling for milk CMV status, a positive association was observed between milk kynurenine and newborn WLZ. This positive association was observed in the CMV-positive and CMV-negative groups; however, it was only statistically significant in the CMV-negative group.

These findings indicate a favorable association between kynurenine abundance in milk and infant one-month WLZ. However, a negative association was observed between CMV counts and one-month WLZ in newborns provided CMV-positive milk.

Conclusion

CMV in breast milk may affect milk composition, neonatal gut flora, and infant growth. CMV transmission, milk composition alterations, or both may also affect long-term infant development. In the current study, consuming CMV-positive milk reduced the levels of beneficial bacteria in the newborn's gastrointestinal tract, which may impact the development of the microbiome.

The study findings emphasize the need for natural variation in human milk for optimal newborn development. Future research is needed to identify kynurenine metabolites and monitor viral transmission.

Source:

https://www.news-medical.net/news/20240728/Cytomegalovirus-in-breast-milk-linked-to-changes-in-infant-growth-and-gut-microbiome.aspx