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Human Milk Oligosaccharides: Potential Upshot on Health at Early Life Stage Development

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Abstract

In the crucial early months of life, an infant's health, growth, and safeguarding are paramount. Breastfeeding stands out as the optimal and natural means of nourishment, offering profound benefits for their development and overall wellness. Within breast milk, a rich array of bioactive components, including hormones, oligosaccharides, and immunoglobulins, provide neonates with an ideal nutritional balance. Among these, Human Milk Oligosaccharides (HMOs) rank prominently, serving both as prebiotics and shields against various neonatal ailments. Particularly, compounds like 2′-Fucosyllactose (2′-FL) and Lacto-N-Neotetraose (LNnT) have been deemed safe for integration into infant formulas, amplifying their benefits. Extensive research underscores the manifold advantages of HMOs, from modulating gut microbiota to bolstering immune function and thwarting pathogenic invaders. HMOs also exhibit a nuanced interplay with maternal genetics, influencing their quantity and diversity. Infants nursed by secretor mothers tend to enjoy enhanced HMO benefits compared to non-secretor counterparts. Incorporating HMOs like Lacto-N-Neotetraose and 2′-Fucosyllactose into infant formulas represents a pivotal stride in optimizing child nutrition. This review offers a thorough exploration of recent research on HMOs, delving into their varied types, concentrations, and compositions, while emphasizing their profound impact on infant health and safety. By consolidating current research findings and recent progress, this study seeks to clarify the diverse effects of HMOs on different facets of human physiology, immune system maturation, modulation of gut microbiota, neurological functioning, and lifelong health implications. Emphasizing the pivotal role of HMOs in influencing human well-being from infancy to maturity, this review emphasize the necessity for continued research and potential utilization in clinical settings and nutritional science.

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Introduction

In accordance with the guidelines established by the World Health Organization (WHO), breast milk is regarded as the best nourishment for infants. It possesses attributes of safety and hygiene and is rich in antibodies that contribute to safeguarding against a multitude of prevalent childhood illnesses (WHO, 2009).[1] Breast milk is a multifaceted constantly-evolving biological fluid that contains both nutritive substances (such as amino acids such as glutamic acid, leucine and proline, proteins, fatty acids such as lactate and succinate, lipids, minerals, carbohydrates, vitamins, etc.) and non-nutritive bioactive substances (such as chemokines, cells, cytokines, immunoglobulins, hormones, growth factors, glycans, mucins, etc.) (Ballard *et al*., 2013).[2] It offers robust defense mechanisms against infections and inflammatory responses, thereby fostering immune maturation, microbiota establishment, organ, and overall infant well-being. Human Milk Oligosaccharides (HMOs) present in breast milk play a pivotal role in bolstering infant immune defenses by promoting the growth of beneficial gut bacteria, which in turn helps prevent infections and inflammation. HMOs also contribute to immune maturation by enhancing the development of the infant's immune system. Moreover, by fostering a healthy microbiota and supporting organ development, HMOs contribute significantly to overall infant well-being, ensuring a strong foundation for long-term health (Hemarajata & Versalovic, 2013).[3] According to the guidelines provided by the WHO and Food and Agriculture Organization in 2001, probiotics are helpful living microorganisms, mainly lactic acid bacteria, that provide a host with a variety of health benefits when consumed in sufficient amounts. Dairy products contain a significant quantity of probiotic bacteria for delivery (Hemarajata & Versalovic, 2013).3 According to several studies food probiotics are a class of functional food products that are widely recognized and accepted by consumers (Al-Sahlany *et al*., 2023).[4] Furthermore, it continues to meet a significant proportion of a child's nutritional needs for 6-12 months, equivalent to approximately half or more of such needs, and up to one-third during the subsequent year of life (IYCF, 2009).[5]

Human breast milk is recognized for its established composition, characterized by approximately 87% to 88% water content and solid components present at a concentration of 124 grams per litre. These solid components comprise macronutrients, including roughly 7% (equivalent to 60–70g/L) carbohydrates, 1% (about 8–10g/L) protein, and 3.8%, indicative of other macronutrients (35–40 g/L) fat (Dror & Allen, 2018).[6] Variations in breast milk's composition may occur as a result of environmental influences, most notably the mother's food intake. Colostrum, the first milk produced after childbirth, has a high percentage of protein but little fat. Additionally, the immune-protective components in colostrum are considerably enriched (Yi *et al*., 2021).[7]

While vitamin levels in breast milk are often sufficient to sustain normal newborn growth, there may be deficiencies in vitamins D and K, needing the infant's supplementation (Balasubramanian, 2011).[8] Several infant formulae closely resemble the composition of human breast milk. These formulations include breast milk-specific ingredients like Human Milk Oligosaccharides (HMOs), which boost their nutritional value (Martin *et al*., 2016).[9] Human Milk Oligosaccharides (HMOs) are the second most prevalent solid and the third most abundant carbohydrate in human breast milk, with lactose ranking first in both categories. They make up about 20% of total carbohydrates in human milk, with mature milk having 12-14 g/L and colostrum having more than 20 g/L (Kim *et al*., 2020).[10]

Composition and Concentration of HMOs

Human breast milk contains approximately fifteen different structural variations of Human Milk Oligosaccharides (HMOs), each distinguished by its unique arrangement and composition of oligosaccharides. The five basic monosaccharides that makeup HMOs are galactose, glucose, sialic acid, fucose, and N-acetylglucosamine. Lactose serves as the terminal (reducing end) component in almost all HMOs. It can be expanded through the addition of Lacto-N-biose I or lactosamine. Linear structures only contain β1–3-linked N-Acetylglucosamine (GIcNAc) residue, while any β1–6-linked N-Acetylglucosamine generates branching within Human Milk Oligosaccharides (HMOs). Incorporating fucose and sialic acid monosaccharides through enzymatic reactions catalyzed by Fucosyltransferases and Sialyltransferases, respectively, might change the sequence of HMOs further by creating alpha 1-2, alpha 1-3, alpha 1-4, and alpha 2-3, alpha 2-6 links (Wiciński *et al*., 2020).[11]

Human breast milk contains human milk oligosaccharides (HMOs), which are complex sugars. The concentrations of HMOs in mature human milk vary between 5 to 20 grams per litre (g/L), with colostrum having significantly higher levels, assuming an energy density of human milk of 64 kcal/100 mL) and 20–25 g/L of colostrum. The HMO content in the human breast milk is more abundant than the protein content, which is typically around 10 g/L (Hegar *et al*., 2019).[12] However, there are observable differences in women's HMO concentrations and profiles. In addition to the influence of the genes producing galactoside 3/4-l-Fucosyltransferase and galactoside 2-l-Fucosyltransferase 2, nothing is known about the underlying causes causing this diversity. These genes influence whether α-1-2-fucosylated and α-1-3/4-fucosylated HMOs are present or absent, but additional variables affecting various HMO forms are still less explored (McGuire *et al*., 2017).[13]

Types of HMOs (Figure 1)

- Fucosylated or Neutral HMOs:"These HMOs contain fucose at the end point such as: "2-Fucosyllactose (2'-FL) and lacto-N-fucopentaose.
- "Non-fucosylated or Neutral N-containing HMOs: These HMOs, like Lacto-N-Tetraose, have N-acetylglucosamine at the endpoint.
- "Acidic or sialylated HMOs:"The terminal end of certain HMOs, such as 2'-sialyl lactose, contains sialic acid.

Within the initial three months postpartum, there is a decline in the overall concentration of Human Milk Oligosaccharides (HMOs). Results showed that the concentrations of individual HMOs are variable depending on the lactation period and dynamic throughout lactation. Most individual HMOs exhibited a tendency to decrease or remain stable after colostrum while 3-FL exhibited increase after colostrum (Soyyılmaz *et al*., 2021).[14] Although there are currently more than a hundred different HMOs, it is important to realize that not all women synthesize the same kinds of oligosaccharides. This unpredictability results from the interaction of numerous elements (Ray *et al*., 2019).[15]

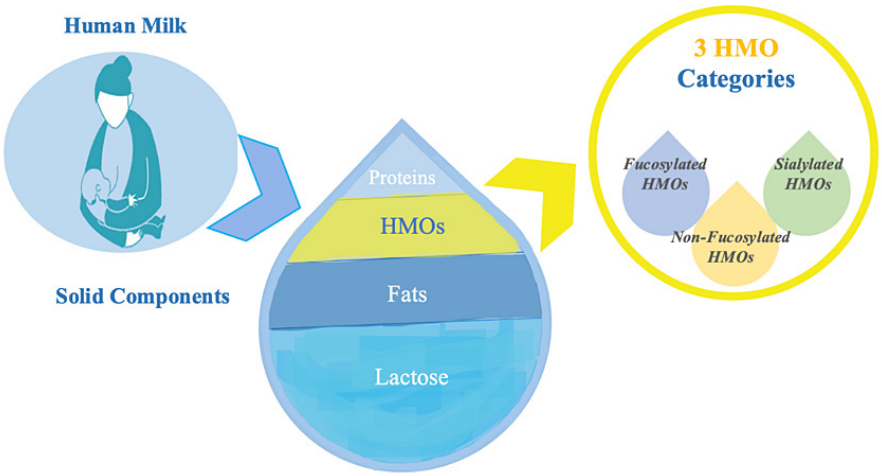

Fig.1: Types of Human Milk Oligosaccharides

The aim of this review paper is to provide a comprehensive overview of the role of human milk oligosaccharides (HMOs) in human development and health. Through synthesizing existing literature and recent advancements, this paper intends to elucidate the multifaceted impacts of HMOs on various aspects of human physiology, including immune system development, gut microbiota modulation, neurological function, and long-term health outcomes. By highlighting the significance of HMOs in shaping human health from infancy through adulthood, this review aims to underscore the importance of further research and potential applications in clinical practice and nutrition science.

Therapeutic Potential of Hmos

Human milk oligosaccharides (HMO) are thought to serve a variety of biological functions in addition to supplying the infant with nourishment. HMO's hold exciting therapeutic potential due to their ability to protect against allergies. Human Milk Oligosaccharides (HMOs) are a particular kind of polysaccharide that may impact the composition of the gut microbiota, strengthen the intestinal epithelial barrier, and triggering immune system regulation. These cumulative effects result in a lower susceptibility of infants to allergies. HMO supplementation has the potential to change the gut microbiota and improve symptoms of irritable bowel syndrome (IBS), through the growth of *Bifidobacterium*.

HMOs and Prebiotics

Prebiotics are dietary substances that, typically in the form of oligosaccharides, regulate the diversity and activity of the microbiota in the human gut to benefit the host organism (Barile & Rastall, 2013).[16] Numerous *in vitro* tests have demonstrated the ability of *Bifidobacterium* species to survive on HMOs. One of the major elements affecting newborn immune development and gut microbiota composition is this sort of commensal feeding. The gut, where most HMOs are broken down into short-chain fatty acids by certain bacteria, which produces an acidic environment. Other helpful *Bifidobacterium* strains survive in the gut's low pH environment (Chichlowski *et al*., 2012).[17]

HMOs function as prebiotics and promote the growth of *Bifidobacterium* species, which is essential for the health of infants. This makes it easier for Bifidobacteria to outcompete dangerous microbes in the newborn's digestive system, preventing infections. A study by (Okburan & Kızıler, 2023)[18] reveals that some *Bifidobacterium* strains have unique enzymatic and genetic processes that allow them to use HMOs as growth media. Recent research, however, indicates that there is still uncertainty regarding the relationship between these bacteria's total metabolic activity and their capacity to metabolise HMOs. *Bifidobacterium longum subsp. infantis* has evolved specifically to metabolize Human Milk Oligosaccharides (HMOs) in the infant gastrointestinal tract, according to genomic research. *Bifidobacterium longum subsp. infantis* renders efficient utilization of both Type 1 and Type 2 Human Milk Oligosaccharides (HMOs) (Garrido *et al*., 2016).[19] The coevolution of humans and *Bifidobacterium* is thought to be due to the presence of type 1 structures in human milk oligosaccharides (HMOs) and the bacterial species' continued use of the Galacto-N-biose/ Lacto-N-biose metabolic pathway (Sakanaka *et al*., 2019).[20] The consumption patterns of Human Milk Oligosaccharides (HMOs) using mass spectrometry-based glycoprofiling revealed a distinct preference for fucosylated oligosaccharides by *Bacteroides vulgatus* and *Bifidobacterium longum subsp. infantis* (Smith-Brown *et al*., 2016).[21]

HMOs and Infant Anthropometry

Anthropometric assessments, including measurements of head circumference, body length (height), and, body weight are recommended for infants and toddlers under the age of two during each well-child visit (Casadei & Kiel, 2022).[22] Reported studies have investigated the relationship between human milk oligosaccharides (HMOs) and infant growth parameters. The first study observed that elevated concentrations of total HMOs were positively correlated with increased levels of infant Fat-Free Mass Index and Fat-Free Mass, while displaying negative associations with Fat Mass, Percentage of Fat Mass, Fat Mass to Fat-Free Mass ratio, and Fat Mass Index (Alderete *et al*., 2015).[23] Consumption of 2′-fucosyllactose (2′FL), 3-fucosyllactose (3FL), difucosyllactose (DFLac), difucosyllacto-N-hexaose (DFLNH), difucosyllacto-N-tetrose (DFLNT), and lacto-N-neohexaose (LSTb) exhibited good relationships with infant's body composition measurements, regardless of maternal secretor status. Certain associations, however, were altered by secretor status. In infants born to secretor mothers, intake of 3'-sialyllactose (3′SL) was positively associated with body composition, but consumption of 6′-sialyllactose (6′SL) and fucodifucosyllacto-N-hexaose (FDSLNH) was adversely associated with body composition. For instance, Sialyllacto-N-tetraose a was positively correlated with weight-for-length z-score but not with weight-for-age z-score in infants. However, another study found no link between Lacto-N-Fucosylpentose I and infant growth in the first four months but suggested lower anthropometric measurements were associated with higher levels of this HMO. The ingestion of various HMOs showed associations with newborn body composition regardless of maternal

secretor status, but differences based on secretor status were noted, such as the positive correlation between 3'-Sialyllactose consumption and body composition in infants born to secretor mothers (Cheema *et al*., 2022).[24]

Human Milk Oligosaccharides and Immune Competence Development

The immune system of neonates differs significantly from that of adults due to its functional immaturity and its distinctive qualitative and quantitative composition (Georgountzou & Papadopoulos, 2017).[25] The distinctions are significant for newborns under a month old since breastfeeding slows the spread of infectious illnesses, which affects the newborns chance of survival. According to Yu *et al*., 2018[26] an newborn's immune system matures significantly throughout the first six months of life, especially if the infant is breastfed exclusively. There is proof that type 1 diabetes, leukaemia, inflammatory bowel disease, allergies, asthma, and other conditions are less common in children who are exclusively breastfed (Liljendahl *et al*., 2022).[27] Human milk oligosaccharides (HMOs) have the potential to affect infants' immune systems. The infant's immune system may be indirectly impacted by the microbiome makeup and epithelial cell responses mediated by HMOs. Human milk oligosaccharides have also directly affected the immune response, (Wiciński *et al*., 2020).11 HMOs may have local and systemic effects on lymphoid tissue cells related to the mucosa because 1% of them are absorbed and circulate throughout the body. Hence it is thought that eating HMOs can have a direct impact on the immune system (Jakaitis & Denning, 2014).[28]

Human milk oligosaccharides (HMOs) help shape the infant gut microbiota and influence immune system development. They have systemic immunomodulatory effects via improving gut health and barrier function, changing gene expression, surface glycans, cytokine production, and immune cell populations. HMOs may function as immune system receptors, regulating mucosa-associated lymphoid cells and influencing dendritic cell cytokine production, so improving both innate and adaptive immunity. Specific HMOs, such as 2'-fucosyllactose (2'-FL) and 3'-sialyllactose (3'-SL), have been found to stimulate Th1 immune responses and increase protection against respiratory viral infections, including better responses to influenza vaccination. Furthermore, 2'-FL treatment improves mucosal barrier function by lowering permeability and upregulating tight junction proteins, which promotes overall immunological health (Dinleyici *et al*., 2023).[29] Plaza-Daz *et al*. (2018)[30] reported that the effects of HMOs on immune cells were studied using intestinal epithelial cells and HeLa cells as cellular models. The study's findings included a characterization of the networks in charge of immune system differentiation, immune cell communication, and homeostasis in the intestinal mucosa (Wang *et al*., 2014).[31] Furthermore, HMO use was found to reduce cytokine protein levels such as Monocyte chemoattractant protein 1/2, IL-6, IL-8, IL-1, and Monocyte chemoattractant protein-1/2. On the contrary, the amount of cytokines associated with tissue repair and homeostasis increased (Rousseaux *et al*., 2021).[32]

HMOs and Infection Illness

HMOs stand out from other compounds because of their prebiotic effect, which promotes the growth of good microbiota over harmful microorganisms. Furthermore, these substances might prevent pathogen adherence and colonisation. The interaction of pathogen receptors and glycans on the surface of human epithelial cells is required for microbial adhesion (Wiciński *et al*., 2020).[11] In this context, the association of HMOs and human milk glycoconjugates, such as glycoproteins and glycolipids, is critical. They work together to reduce pathogen adherence. Because they are structurally similar to surface glycans on epithelial cells, HMOs and glycoconjugates are recognized and bound by either bacterial lectin receptors or rapidly dividing epithelial cells. In both instances, this limits the colonization of pathogens (Pacheco *et al* ., 2015).[33] Purified HMOs have the ability to inhibit the growth of bacteria such as *Acinetobacter baumannii, Streptococcus agalactiae and Staphylococcus aureus*. Notably, Lacto-N-triose II (LNT-II), a critical structural component in the synthesis of various human milk oligosaccharides, exhibited the most potent antimicrobial activity against *Streptococcus agalactiae* (Ackerman *et al*., 2018).[34] Fucosylated and Sialylated milk oligosaccharides decrease the frequency and intensity of gastrointestinal infections by blocking interactions between pathogens and host receptors, as evidenced by research findings for *Norovirus, Campylobacter, Escherichia coli and* Rotavirus (Corona *et al*., 2021).[35]

In terms of preventing respiratory tract infections, adding 2-Fucosyllactose and Lacto-N-Neotetraose to a standard formula correlates with fewer occurrences of bronchitis and medication use as reported by parents. Instead, HMOs interfere with hemagglutination, which enhances the innate immune response to influenza viruses (Cohen *et al*., 2016).[36] Only 10-15% of infants who are nursed by HIV-positive mothers get the infection, Indicating that the bioactive properties of HMOs might be a contributing factor to atypical HIV transmission through breastfeeding, higher levels of HMOs are associated with reduced postnatal HIV transmission risk in infants who are breastfed because they may prevent HIV from attaching to intercellular adhesion molecules unique to dendritic cells; specialized antigen-displaying cells that help in the fight against invasive pathogens while promoting tolerance to one's own and safe environmental antigens (Wahl *et al*., 2015).[37]

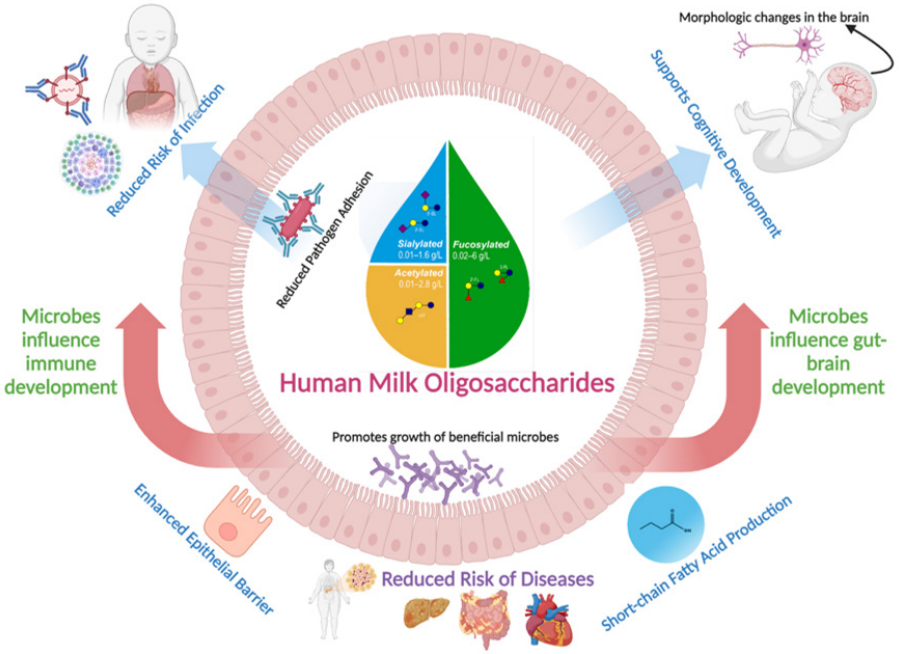

Fig. 2: Potential impacts of HMOs

HMOs and Cognitive Development

The initial half-year of an infant's life is characterized by swift cerebral expansion, necessitating an elevated requirement for particular nutrients to support neurocognitive maturation. The benefits of exclusive breastfeeding have been amply documented throughout this time, which also falls within the WHO guidelines (Brown, 2017).[38] In fact, it has been discovered that breastfed neonates do better on "intelligence test scores" throughout infancy, with consequences for maturity as well. Hence, there exists a critical period during early developmental phases where the promotion of proper brain maturation can align with a diet known for its profound influence.

Considering that neurons' cell membranes predominantly comprise sialic acid, recent findings have underscored the significance of sialylated oligosaccharides, specifically sialylated HMOs, in neurological development. Glycosphingolipids, which have a hydrophilic head made of sialylated oligosaccharides, are essential parts of gangliosides, these compounds participate in various neurodevelopmental processes, including synaptic transmission, memory formation, cognitive function, and the acquisition of learning (Corona *et al*., 2021).[35] The concentration of gangliosides in the brain triples from 1 trimester of pregnancy to 5 years of age of a child, providing additional evidence

for the importance of this molecule during the early developmental stages of life (Palmano *et al*., 2015).[39]

HMOs and Allergies

The intricate interconnected pathways that HMOs provide alter an individual's susceptibility to allergies through their prebiotic properties and immune-modulating effects. The normal microbiota and microbiome contain short-chain fatty acids such as butyrate and propionate, that possess properties that can combat allergies and inflammation. These qualities contribute significantly to immune enhancement by reducing the prevalence of allergic disorders (Rey-Mariño & Francino, 2022).[40] These substances reduce the chance of developing asthma and food allergies. In mice exposed to household dust, reduced gut microbial short-chain fatty acid synthesis is correlated with greater immunoglobulin E (IgE) levels, goblet cell hyperplasia, elevated mucus within the respiratory passages. Asthma and allergic dermatitis appear to be prevented by species like *Bifidobacterium longum* (Corona *et al*., 2021).[35]

Impact of Maternal Health on HMOs Component

Women with a BMI of 14 kg/m^2 to 18kg/m^2 had considerably lower HMO concentrations compared to women with a BMI of 24kg/m^2 to 28kg/m^2. Individual HMO levels may be influenced by pre-pregnancy BMI and prenatal weight gain, as per findings from the ATLAS cohort study involving mothers from Europe. The impact of these on the HMO concentrations, however, were minimal. Pregnancy-related gestational diabetes did not alter the volume or make up of all HMOs (Biddulph *et al*., 2021).[41]

Safety

Oligosaccharides in human milk have been scientifically known to stimulate the growth of *Bifidobacterium* since the 1930s. By 1954, the most common oligosaccharides in breast milk had been identified. In recent years, a small amount of Human Milk Oligosaccharides (HMOs) has been successfully produced on an industrial scale. The molecular composition of industrially produced Lacto-N-Neotetraose and 2'-Fucosyllactose is very similar to that of oligosaccharides found naturally in human breast milk. Notably, unlike probiotics, HMOs support freeze-drying and pasteurization (Hegar *et al*., 2019).[12] Two intervention trials were carried out to assess the safety of an infant formula containing approximately 0.2 g/L 2'-fucosyllactose. The addition of 2 g/L fucosyllactose in combination with galacto-oligosaccharides was well tolerated, had no effect on growth parameters, and had no effect on stool frequency or consistency (Alliet *et al*., 2022).[42]

Table 1: HMOs functions reported in literature

Authors	Study Objectives	Study Outcomes
Ray *et al*[15]	"Human Milk Oligosaccharides: The Journey Ahead"	As a key element of the immunological defence provided by breast milk to weak babies, HMOs offer the next frontier in neonatal nutrition. The specific HMOs to be employed must be identified through fundamental scientific research, and clinical evidence should validate the need to complement infant formula with these components.
Hegar *et al*[12]	"The Role of Two Human Milk Oligosaccharides, 2′-Fucosyllactose and Lacto-N-Neotetraose, in Infant Nutrition"	"HMOs improve the responsiveness of neonatal epithelial and immune cells by preventing bacterial, viral, or pathogens from binding to epithelial cell receptors. As per the study, 2'-Fucosyllactose (2'-FL) is deemed a safe supplement for infant formula, exhibiting no adverse effects on the gut flora of newborns fed with a formula enriched with this compound."

Wiciński *et al*[11]	Human Milk Oligosaccharides: Health Benefits, Potential Applications in Infant Formulas, and Pharmacology”	Intake of HMOs through breastfeeding is critical for of various immune-related disorders like celiac disease, acute lymphoblastic leukemia, allergies, type 1 diabetes, asthma, and acute myeloid leukemia.
Corona *et al*[35]	“Human Milk Oligosaccharides: A Comprehensive Review towards Metabolomics”	“Distinguished by its intricate and dynamically evolving composition, breast milk confers profoundly beneficial effects on the health and developmental trajectory of neonates and infants, yielding substantial long-term advantages for both the progeny and adults. Research has documented the physiological and protective attributes of Human Milk Oligosaccharides (HMOs), including their contributions to brain and intestinal development as well as bolstering resistance against infections.”
Zhang *et al*[44]	“Gold standard for nutrition: a review of human milk oligosaccharide and its effects on infant gut microbiota”	HMOs affect not just infants but also babies and adults. In a separate investigation, it was observed that after a three-week regimen of 2'-Fucosyllactose (2'-FL) treatment, Caco-2 BBE cells demonstrated a reduction in monolayer permeability and an elevation in the expression levels of tight junction proteins, specifically claudin-5 and claudin-8. This enhancement contributed to the fortification of the mature intestinal barrier.
Sprenger *et al*[45]	“Biology of human milk oligosaccharides: From basic science to clinical evidence”	HMOs exhibit a variety of structure- and function-specific behaviors that are only seen with particular HMO species and seldom with unrelated glycans that are frequently utilized as prebiotics. Although the quantities and structural diversity of HMOs are notably abundant in human milk, some oligosaccharides are found in all animal milks.
Zhang *et al*[46]	“Human milk oligosaccharides and infant gut microbiota: Molecular structures, utilization strategies and immune function”	Infants' gut microbiome and immune system are significantly influenced by gut bacteria such as *Bifidobacterium, Bacteroides, and Lactobacillus* during the absorption and metabolic processes of Human Milk Oligosaccharides (HMOs). This is essential to the manifestation of the benefits of HMOs that promote health.
Mills *et al*[47]	“Translating neonatal microbiome science into commercial innovation: metabolism of human milk oligosaccharides as a basis for probiotic efficacy in breast-fed infants”	The emergence of "omics" technologies, particularly next-generation sequencing, which opens the door to previously unknown microbial communities, has resulted in an explosion of data about our gut microbiome and its function. Newborn’s consumption of HMOs by Bifidobacterium probiotics is a novel, targeted application where the probiotic's direct function is plain to see.

Significant findings included a decrease in lower respiratory tract infections up to the 12-month mark, as well as a decrease in the occurrence of bronchitis at 4, 6, and 12 months, a decreased reliance on antipyretics for the first 4 months, a decrease in antibiotic use at the 6- and 12-month intervals, and the persistence of protective effects beyond the 6-month post-intervention period among infants who received supplements containing 2-fucosyllactose and La (Fiocchi *et al*., 2021).[43]

Future Prospects and Constraints

The future prospects for utilising the benefits of human milk oligosaccharides (HMOs) in newborn development are promising with current research emphasizing their critical role in forming gut microbiota and boosting immune function. HMOs have the potential to improve infant health outcomes by lowering the risk of infection and encouraging healthy growth and development. However, obstacles like as the complexity of HMO structures, difficulties in large-scale manufacture, and regulatory concerns must be overcome. Efforts to overcome these barriers, together with ongoing advances in biotechnology and formulation science, could open the way for the broad introduction of HMOs into infant feeding products, ultimately improving the health and well-being of infants globally.

Further research into the unique health benefits of human milk oligosaccharides (HMOs) holds promise for the development of novel infant formulae supplemented with HMOs that closely resemble the composition of human breast milk. HMOs may have implications beyond infant nutrition, such as functional foods and dietary supplements that improve gut health and immunological function in both infants and adults. HMOs (Human Milk Oligosaccharides) and oligosaccharides isolated from animal milk, such as bovine milk, exhibit similarities in their prebiotic effects and potential immunomodulatory properties. However, they differ significantly in their structural composition, source, and specific functional benefits due to their tailored roles in human and animal nutrition respectively. HMOs have inherent therapeutic potential, including the ability to alter gut microbiota and immunological responses, and may present innovative paths for treating a variety of health issues, including gastrointestinal illnesses and immune-related diseases. Commercial infant formulas now include added HMOs to better resemble breast milk. Marketed as "HMO-added" or "HMO-enriched," these formulas aim to mimic breast milk's nutritional benefits, though they may not match its composition entirely. Ongoing research means formulations may evolve. For the latest, consult manufacturers or recent infant nutrition literature. Biotechnology advancements may make it possible to produce HMOs at a lower cost by microbial fermentation or enzymatic synthesis, increasing availability to these beneficial substances. However, the structural complexity of HMOs complicates their isolation, characterisation, and synthesis, necessitating the development of efficient large-scale manufacturing and purification techniques. Regulatory clearance processes for novel food components and therapeutic treatments, including HMOs, are stringent and time-consuming, emphasising the significance of establishing safety and efficacy in order to acquire commercial acceptability.

Conclusions

HMOs occupy a distinct position in disease prevention and treatment, thereby upholding the well-being of both pediatric and adult populations. Findings on HMO's are the newest development in neonatal nutrition and fulfil a substantial function in the immunological protection that breast milk offers to vulnerable neonates. The advancement of research and applications in infant feeding and therapeutics depends on resolving critical challenges with the isolation of Human Milk Oligosaccharides (HMOs). Human milk oligosaccharides (HMOs) are difficult to isolate because of their complex structures, low breast milk quantities, and high purity requirements. The main challenges include addressing ethical issues, scaling up production while keeping cost efficiency, and achieving specificity without adding contaminants. Clinical research has advanced to the point that it now views HMOs as a favourable option for infants unable to receive breastfeeding. Even though research has contributed to advanced knowledge, substantial issues with isolating human milk oligosaccharides still need to be solved. These problems include increasing purity while lowering contamination, developing scalable and economical processes, and advancing structural characterization to achieve the full potential of these molecules in infant nutrition and therapeutics.

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Competing Interest
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Authors' Contribution
Neelam Chaturvedi: detailed conceptualization and writing of original draft, formulation of methodology, reviewing, editing and supervision; Bhargavi Gupta: writing-original draft and reviewing; Neha Sahrawat: conceptualized the original draft, formulated methodology, reviewed and edited the manuscript; Saloni Dua: gathered sources, reviewed and edited the manuscript; Chandra Kumari: edited the original draft and Srishti Mittal: writing-original draft.

Data Availability Statement
Not applicable

Ethics Approval Statement
Not applicable

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