

Original Research Article

Evaluating clinical opinions on the efficacy and tolerability of a novel human milk oligosaccharide-based human milk fortifier containing lactoferrin, docosahexaenoic acid and arachidonic acid

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ABSTRACT

Background: To gather and analyse the opinions of healthcare professionals regarding the effectiveness and tolerability of a novel human milk oligosaccharide (HMO)-based fortifier containing lactoferrin, docosahexaenoic acid (DHA) and arachidonic acid (ARA) in neonatal nutrition.

Methods: A cross-sectional survey was conducted among neonatologists and paediatricians who have utilised the novel HMO-based human milk fortifier (HMoF) in their clinical practice. Participants were asked to provide their feedback on various parameters including nutritional adequacy, growth outcomes, tolerance, and overall clinical efficacy.

Results: Majority of respondents reported positive outcomes in terms of enhanced growth parameters, improved gastrointestinal tolerance, and overall health of the infants. The fortifier was particularly noted for its role in supporting the overall growth of the infants including weight gain, length gain and head circumference gain due to the presence of HMOs, lactoferrin, DHA, and ARA.

Conclusions: The novel HMO-based human milk fortifier containing lactoferrin, DHA, and ARA has garnered a favourable and positive opinion by healthcare professionals and demonstrates potential benefits in enhancing neonatal nutrition and health outcomes.

Keywords: Growth, Human milk fortifier, HMOs, Preterm babies

INTRODUCTION

Human milk oligosaccharides (HMOs) are essential components of breast milk, playing a crucial role in infant nutrition and immune system development. They serve as prebiotics, promoting the growth of beneficial gut bacteria, and have been shown to protect against pathogens and support immune function¹. Recent advances in neonatal nutrition have led to the development of HMO-based fortifiers (HMoF) aimed at mimicking the natural benefits of breast milk.²

Lactoferrin, a multifunctional protein found in high concentrations in human milk, has potent antimicrobial and anti-inflammatory properties.

It also plays a significant role in iron metabolism and the modulation of the immune response.^{3,4} DHA and ARA are long-chain polyunsaturated fatty acids critical for brain and eye development in infants.⁵

This study aims to evaluate the clinical opinions of healthcare professionals on the efficacy and tolerability of a novel HMoF containing lactoferrin, DHA, and ARA.

METHODS

Study design

A cross-sectional survey was conducted from May to July 2024 involving 115 participants.

Participants

Neonatologists and Paediatricians from various healthcare settings were invited to participate.

Inclusion criteria included having experience using the HMoF in clinical practice.

Survey instrument

A structured questionnaire was designed on Google forms to collect data on the participants' experience with the HMoF. The questionnaire included items on: Name of Hospital and field of speciality, use of the fortifier, gastrointestinal tolerance, observations on infant growth parameters (weight, length, head circumference) and overall clinical efficacy and satisfaction

Data analysis

Descriptive statistics were used to summarize the data. Qualitative responses were analysed thematically to identify common themes and patterns. Statistical analysis was done using IBM SPSS statistics v21 software.

Consent

Consent to participate in the study was obtained from each participant through the Google form.

Funding

No funding has been obtained for the study from any source.

Ethical considerations

No incentives or compensation were provided to the participants and participants have provided their opinion based on their experience only.

RESULTS

Demographic information

A total of 115 healthcare professionals participated in the survey.

The majority were neonatologists (78%), followed by paediatricians (22%). Participants were spread across 27 cities and 88 hospitals.

Table 1: Demography of participants, (n=115).

Variables	Neonatology	Paediatrics
Speciality of participants	90	25
Percentage (%)	78	22

Feed volume at which fortification initiated with novel HMoF

45% of the participants reported having initiated fortification with HMoF at feed volume of 101-150 ml while another 41% reported the same at feed volume of less than 100 ml. Another 14% also reported having initiated fortification at feed volume of more than 150 ml.

Table 2: Feed volume at which fortification initiated with novel HMoF (n=115).

Feed volume (ml/kg/day)	N	Percentage (%)
Less than 100 ml	47	41
101-150 ml	52	45
More than 150 ml	16	14

Gestational age (GA) of infants at which fortification recommended with novel HMoF

44% of the participants reported having recommended fortification with HMoF to infants at GA between 30-32 weeks while another 30% reported the same at GA of 30 weeks or lesser. Another 26% also reported having recommended fortification at GA of more than 32 weeks. Some of participants made one or more than one choice on this parameter.

Table 3: GA of infants at which fortification recommended with novel HMoF, (n=115).

GA of infants	N	Percentage (%)
30 weeks or lesser	42	30
Between 30-32 weeks	61	44
More than 32 weeks	36	26

Average weight of the infants to whom fortification recommended with novel HMoF

Majority of the participants (53%) reported having recommended fortification with HMoF to infants at average weight of 1000-1500 gm. Some of participants made one or more than one choice on this parameter.

Table 4: Average weight of infants at which fortification recommended with novel HMoF, (n=115).

Average weight of infants	N	Percentage (%)
Less than 1000 gm	20	15
1001-1500 gm	71	53
1501-2000 gm	22	17
2001-2500 gm	20	15

Clinical observation of tolerability amongst preterm infants on fortification with novel HMoF

Observation of respondents was solicited in terms of experience with HMoF in terms of tolerability observed on a 3-point scale of meets expectations, exceeds expectations, and lower than expectations.

Table 5: Clinical observation of tolerability amongst preterm infants on fortification with novel HMoF, (n=115).

Experience in terms of tolerability	N	Percentage (%)
Meets expectations	85	74
Exceeds expectations	26	23
Lower than expectations	4	3.5

Majority of the respondents, 74% observed that HMoF meets expectations of tolerability, while another 23% observed that HMoF exceeds expectations. This observation is supported by the prebiotic effects of HMOs, which enhance the gut microbiota composition and function⁶. A very small percentage of 3.5% opined that the same is lower than expectations.

Clinical observation on growth outcomes (weight gain, length gain and head circumference gain) of preterm infants on fortification with novel HMoF

Observation of respondents was solicited in terms of growth outcomes such as weight gain, length gain and head circumference gain on a 3-point scale of meets expectations, exceeds expectations, and lower than expectations.

Table 6: Clinical observation on growth outcomes of preterm infants on fortification with novel HMoF, (n=115).

Experience in terms of growth outcomes	N	Percentage (%)
Meets expectations	93	81
Exceeds expectations	19	17
Lower than expectations	3	3

Majority of the respondents, 81% observed significant improvements in infant growth parameters, including weight gain, length gain and head circumference gain. Another 16.5% observed that fortification with HMoF exceeds expectations. These findings align with previous studies indicating that DHA and ARA supplementation supports healthy growth in preterm infants.⁷ A very small percentage of 2.6% opined that the same is lower than expectations.

Clinical observation on ingredients of novel HMoF instrumental for improved tolerability amongst preterm infants

The novel HMoF is novel due to presence of specialised ingredients such as HMOs, lactoferrin, hydrolysed whey, DHA and ARA. Another important aspect of the HMoF is in it being maltodextrin free. These factors play a critical role in improving feed tolerability and preventing gastrointestinal intolerance.

Table 7: Clinical observation on ingredients of novel HMoF instrumental for improved tolerability, (n=115).

Ingredients instrumental for improving tolerability	N	Percentage (%)
Zero maltodextrin	2	2
Lactoferrin	4	4
HMOs	8	7
Hydrolysed whey	10	9
All of these	91	79

Majority of the respondents, 79% observed that improved tolerability is a factor of all the specialised ingredients while few respondents also observed that the same is attributed to specific ingredients.

Clinical observation on ingredients of novel HMoF instrumental for improved growth outcomes of preterm infants

30% protein content, protein in the form of lactoferrin and protein energy ratio of 3.5 are key factors for promoting the growth outcomes of preterm infants including weight gain, length gain and head circumference gain.

Table 8: Clinical observation on ingredients of novel HMoF instrumental for improved growth outcomes, (n=115).

Ingredients instrumental for improving growth outcomes	N	Percentage (%)
Protein in form of lactoferrin	2	2
Protein: energy ratio of 3.5	10	9
30% protein content	12	10
All of these	91	79

Majority of the respondents, 79% observed that improved tolerability is a factor of all the specialised ingredients while few respondents also observed that the same is attributed to specific ingredients.

Clinical observation on weight gain of preterm infants on fortification with novel HMoF

22-25 gm/day weight gain was recorded by 23% of the respondents, whereas 18-21 gm/day weight gain was

recorded by 50% of the respondents. Another 27% respondents recorded a weight gain of 14-17 gm/day.

Table 9: Clinical observation on weight gain of preterm infants on fortification with novel HMoF, (n=115).

Weight gain per day in grams	N	Percentage (%)
14-17 gm/day	31	27
18-21 gm/day	58	50
22-25 gm/day	26	23

Overall, the respondents expressed satisfaction with the fortifier, citing its comprehensive nutritional profile and positive impact on infant health. The inclusion of HMOs, lactoferrin, DHA, and ARA provides a balanced approach to neonatal nutrition, addressing multiple aspects of infant development.

DISCUSSION

The findings of this study indicate that the novel HMoF is well-received by healthcare professionals, demonstrating significant benefits in neonatal nutrition. The inclusion of lactoferrin, DHA, and ARA appears to enhance gastrointestinal health, growth outcomes and improved tolerability, aligning with existing literature on their individual benefits.

Our findings are also in line with previous studies that have shown the beneficial effects of HMOs, which as bioactive components of human milk, play a pivotal role in shaping the infant gut microbiota and enhancing mucosal immunity.⁸⁻¹¹ Lactoferrin's antimicrobial and anti-inflammatory properties are well-documented, contributing to its effectiveness in preventing infections and promoting gut health.^{12,13} DHA and ARA are critical for brain development, with numerous studies highlighting their importance in cognitive and visual function.^{5,7}

Our findings are also in line with previous studies conducted on novel HMO-based human milk fortifier that have demonstrated that novel HMoF containing lactoferrin, DHA, and ARA is well tolerated by preterm infants, with no reported clinically significant incidences of adverse effects.^{14,15} In addition, novel HMoF containing lactoferrin, DHA, and ARA improved the growth of premature infants at discharge.

The strengths of our study include the use of data from multiple centres that participated in the study, which reduced the uniformity and bias that may arise from single centre. We also used standardized and validated methods to analyse the data captured from the participants.

The limitations of our study include the non-comparative observational design, which precluded causal inference

and increased the risk of confounding. We also had a small sample size and a short follow-up period, which limited the statistical power of our findings. Furthermore, we did not measure other outcomes that may be relevant for premature infants, such as infection rates, hospital readmissions, neurodevelopmental impairment, and quality of life.

CONCLUSION

The novel human milk oligosaccharide based fortifier (HMoF) containing lactoferrin, DHA, and ARA is considered effective by healthcare professionals in improving neonatal growth, gastrointestinal tolerance, immune function, and neurodevelopment. These findings support the fortifier's potential role in enhancing neonatal nutrition and health outcomes.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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