

Feeding practices and the prevalence of cow's milk protein allergy in Irish preterm infants

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Abstract

Background

The prevalence of cow's-milk protein allergy (CMPA) is between 2% and 3% and symptoms vary depending on underlying immune mechanism at play. Breast milk is the optimal nutrition for premature infants and breast milk fortifiers (BMF) are commonly used to optimise growth and nutrition. BMF are typically derived from cow's milk and, as such, preterm infants are exposed to cow's milk in the first weeks of life. Previously, preterm infants were suspected to have a higher risk of allergen development because of early antigen exposure and increased gut permeability. The primary aim of the present study was to evaluate the prevalence of CMPA among very preterm (<32 weeks) and/or very low birth weight (VLBW) infants. The secondary aim was to describe feeding practices, specifically the breastfeeding rates and specialist, non-standard formula use in this cohort over the first 6 months of life.

Methods

This was a retrospective study performed in a large tertiary maternity hospital (8500 deliveries/year and 110 very preterm infants/year) in Dublin, Ireland over a 3-year period, 2017–2020. Infants born very preterm and/or VLBW who were followed in the outpatient clinic until 6 months corrected gestational age (CGA) were included. Hospital ethical approval was obtained.

Results

One hundred and forty-four infants were included with a median birth weight of 1338 g.

No infant had a diagnosis of CMPA when leaving the neonatal intensive care unit (NICU) but, by 6 months CGA, this increased to 1.4% ($n = 2$). Upon discharge from the NICU, 88 infants (61%) were receiving at least some breast milk, decreasing to 13 (9.1%) at 6 months CGA. Those who were receiving exclusive breast milk at discharge were significantly more likely to still be receiving any breast milk at three ($p \leq 0.001$) and 6 months ($p \leq 0.001$) CGA compared to those combined feeding or exclusively formula feeding. At 6 months CGA, 18.9% ($n = 27$) were attending a dietician and 31.5% ($n = 45$) were using specialist, non-standard infant formula.

Conclusions

The prevalence of CMPA in this cohort was 1.4%, which is similar to the reported prevalence of CMPA in the general paediatric population. Infants who were discharged from NICU exclusively breastfeeding were more likely to be receiving any breast milk at outpatient follow-up. This highlights the importance of on going dietetic and lactation support in the outpatient setting for this vulnerable cohort.

Key points

The prevalence of CMPA in our cohort was similar to the previously determined prevalence in the general paediatric population.

The significant use of specialist formula among ex preterm/VLBW infants during the first year of life conveys the need for accessible dietetic services.

Breastfeeding rates were lower in the ex preterm cohort compared to term infants in Ireland. Breastfeeding initiation and support in the NICU is extremely important for sustaining breastfeeding rates at home following discharge.

INTRODUCTION

Cow's milk protein allergy (CMPA) is mainly a disease of early infancy, with presentations largely occurring before 6 months of age.¹ The prevalence of CMPA in children varies in epidemiological studies, ranging from less than 1% in the EuroPrevall study,² to as high as 7%.³ However, it is generally accepted as falling between 2% and 3% and is the most common food allergy in infancy.^{4,5} CMPA is an important public health issue with significant economical, nutritional and quality of life burden for families and clinicians.⁶

CMPA may be stratified into groups determined by underlying pathogenesis: immunoglobulin (IgE) mediated allergy, non-IgE mediated and mixed response, with symptoms most commonly secondary to non-IgE mediated allergy.¹ IgE mediated allergy may present with urticarial, angioedema and anaphylaxis. Presentation of CMPA in non-IgE mediated allergy may be non-specific and chronic, with presentation usually manifesting with gastrointestinal

symptoms, including faltering growth, reflux, feed refusal or aversion, abdominal discomfort, irritability, blood or mucous in stool and/or diarrhoea.³

Diagnostic criteria include history and physical examination with a sequence of symptoms followed by resolution with strict allergen avoidance. Double-blind, placebo-controlled oral food challenge is gold standard,⁷ although this may not always be feasible in practice. Children should be assessed at 6–12-monthly intervals for the development of tolerance to cow's milk and this is achieved in 75% of patients by 3 years of age.⁷

Given the potential non-specific nature of CMPA and significant clinical overlap of symptoms, varying manifestations and level of severity, CMPA remains a diagnostic challenge for clinicians, particularly in the preterm infant.⁸

In Ireland, 4500 babies are born prematurely (<37 weeks) every year, of which over 500 are very low birth weight (VLBW) infants weighing less than 1500 g at birth.^{9, 10}

The final trimester of pregnancy and corresponding neonatal intensive care unit (NICU) period for VLBW infants is the most critical period for brain growth and development. Failure to meet nutritional demands with inadequate nutrition and poor growth during the NICU stay has been associated with adverse neurocognitive outcomes.¹¹

Mother's own milk is the optimum nutrition available for premature infants.¹² However, it does not provide sufficient calories, energy, protein and other nutritional requirements at standard volumes to meet the demands of growing VLBW infants.¹³

To adequately meet the requirements of preterm infants, breast milk fortifiers (BMF) are commonly used to optimise growth and nutrition.¹¹ BMF are typically derived from cow's milk and as such preterm infants are exposed to cow's milk in the first weeks of life. Fortifiers may use whole, partly hydrolysed or extensively hydrolysed cow's milk proteins.¹³ Breast-fed term infants who received cow's milk formula supplementation in the first 24 h of life were found to be more likely to develop CMPA compared to those exclusively formula fed.¹⁴ However, in a study of 324 very preterm infants, supplementation of breast milk with BMF for 4 months of age did not have an increased risk of allergy in the first year of life.¹⁵

Previously, preterm infants were considered to be at higher risk of developing food allergies because of increased gut permeability and early food antigen exposure.¹⁶

A Canadian birth cohort study of 13,980 children found that infants who were less than 28 weeks of gestational age at delivery had an 8.1% frequency of food allergy, falling to 1.2% between 28 and 31+ 6/7 weeks of gestational age. However, it was concluded that there was no association between prematurity or birth weight and the development of IgE mediated food allergy. It was also postulated that early exposure to antigens was in fact a protective factor by increasing immune tolerance.¹⁷ Interestingly, infants born prematurely also have lower rates of atopic dermatitis compared to term counterparts.¹⁸

Reynolds et al.¹⁹ described the first Irish cohort, in which they identified 51 paediatric patients attending their outpatient service, and concluded that their findings were in agreement with international values. The majority presented with non-IgE mediated allergy and all presented before 6 months of age.¹⁹ There is a paucity of Irish studies examining CMPA in the ex premature infant. In the present study, the primary objective was to ascertain the prevalence of CMPA in this cohort, and to determine whether this differed from the documented prevalence in the paediatric population.

In addition, there is little information regarding the feeding practices of premature and VLBW infants following discharge from hospital. Only 37% of Irish infants are exclusively breast-feeding on discharge from hospital, although this value does not differentiate for gestational age.²⁰ We aimed to examine breastfeeding rates and the use of specialist formulas at three and 6 months of corrected gestational age (CGA).

METHODS

We carried out a retrospective cohort study of all infants born <32 weeks of gestational age and/or <1500 g and admitted to the NICU in the Rotunda Hospital, a large tertiary maternity hospital in Dublin, Ireland with 8500 deliveries/year and 110 very preterm infants/year. These patients were identified using hospital inpatient enquiry database and medical records. The information was accessed from the electronic health record. Regular follow-up of ex-premature infants is standard practice in our institution. They are typically reviewed in a Neonatology consultant led clinic at term, and 3 and 6 months CGA. These infants are routinely followed up until 2 years of corrected age.

Infants were included if they were born between 1 November 2017 and 31 October 2020. We excluded neonates who did not survive to discharge, transfers to outside hospitals and infants who did not have follow-up until 6 months CGA.

Parameters analysed included patient demographics (gender, gestational age, birth weight, weight centile at birth and discharge), time to first enteral feed and initial feed used (maternal breast milk, donor breast milk and/or specific formula type). Feeding practices were also recorded at discharge from the NICU, and at outpatient review at 3 and 6 months CGA. A chart review was performed on all included infants. Prevalence of CMPA was assessed as per the International Milk Allergy in Primary Care (iMAP) Guideline.²¹ Infants with symptoms suggestive of IgE (anaphylaxis, urticaria, angioedema) and/or non-IgE mediated CMPA (irritability, vomiting, reflux, gastrointestinal reflux, blood and/or mucous in stool, abdominal discomfort, diarrhoea, skin rashes) and resolution of symptoms with a cow's milk free diet, either by maternal elimination of cow's milk products if exclusively breastfeeding or use of extensively hydrolysed formula (eHF) subsequently followed by, if required, an amino acid formula (AA), were included.

Data were extracted from the Electronic Patient Record and anonymous data was collected

in Excel (Microsoft Corp.). Descriptive statistics were performed. Stata SE, version 16.0 (StataCorp) was used for statistical analysis. For continuous variables, the mean (SD) and median (25th–75th percentile, interquartile range [IQR]) are described for normal and non-normal distribution, respectively. For categorical variables, frequency (percentages) are described. Fisher's exact test was used to test the significance of categorical variables. $p < 0.05$ (two-sided) was considered statistically significant.

The Rotunda Hospital Research and Ethics Committee granted approval for this retrospective study (approval number 2020-034).

RESULTS

Following implementation of inclusion and exclusion criteria, 144 infants were included in the study: 73 males and 71 females. The median birth weight and centile of the group was 1338 grams (IQR 965–1595 g) and 54th centile. The median gestational age at birth of infants included was 30.1 weeks (IQR 27.6–31.3 weeks). Forty-three infants (29.9%) were less than 28 weeks of gestational age at birth.

Type of first feed was reviewed, 71% ($n = 102$) received maternal expressed breast milk, 13.9% preterm ($n = 13$) formula and 8.3% ($n = 12$) donor expressed breast milk (Table 1).

Table 1. Patient demographics and characteristics of the sample

<i>Patient demographics</i>	
Male:Female	73:71
Gestational age, median (IQR)	30.14 (27.6–31.3) weeks
<28 weeks of gestation	43 infants
>28 weeks of gestation	101 infants
Birth weight, median (IQR)	1338 (965–1595) g
Birth weight centile, median (IQR)	53.8 (33.8–73.4) centile
Time at first feed, median (IQR)	10.5 (6–20) h
Discharge weight centile, median (IQR)	32.7 (17–50.5) centile
Type of first feed, n (%)	
– Maternal expressed breast milk (EBM)	102 (70.8)
– Preterm formula	20 (13.9)
– Donor EBM	12 (8.3)

– EBM (not specified)	4 (2.8)
– Soy-based formula	4 (2.8)
– Unknown	2 (1.4)

Abbreviation: IQR, interquartile range.

No infant had a diagnosis of CMPA at discharge from the NICU. Two infants were receiving an eHF secondary to a history of necrotising enterocolitis (NEC) and ileostomy formation.

At discharge from hospital, 61% ($n = 88$) were receiving any/some breast milk, of which 46 infants were exclusively receiving breast milk, and a further 42 infants were combination fed (Figure 1). Preterm post discharge formula was used by 65% of all infants at discharge ($n = 93$) and was the most commonly used formula at 95.9%. The median weight centile at discharge was the 32nd centile (IQR 17th–51st centile).

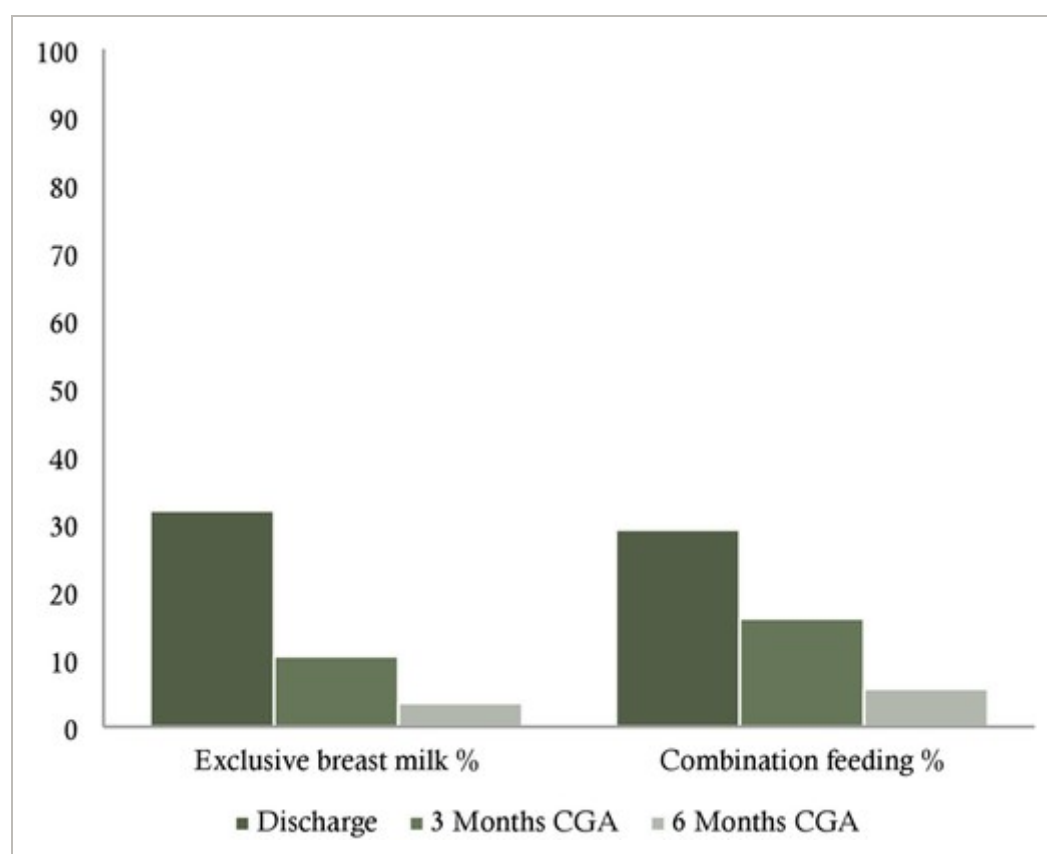


Figure 1

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Provision of breast milk (exclusively and combined) at discharge, 3 and 6 months corrected gestational age (CGA) follow-up

At outpatient review at 3 months CGA (IQR 1.5–3 months CGA), 26.4% ($n = 38$) were receiving

any/some breast milk and 10.4% ($n = 15$) were exclusively receiving breast milk. (Figure 1). In this cohort, 67.6% ($n = 96$) were exclusively formula fed. Again, preterm post discharge formula was the most common formula used ($n = 71$). Almost all, 95% ($n = 138$), had not yet started solids.

At 6 months CGA, one infant did not have their feed type recorded. Of the 143 infants, only 9.1% ($n = 13$) were receiving any/some breast milk, with 3.5% ($n = 5$) exclusively receiving breast milk (Figure 2). No further diagnoses of CMPA had occurred subsequent to the previous review at 3 months CGA ($n = 2$).

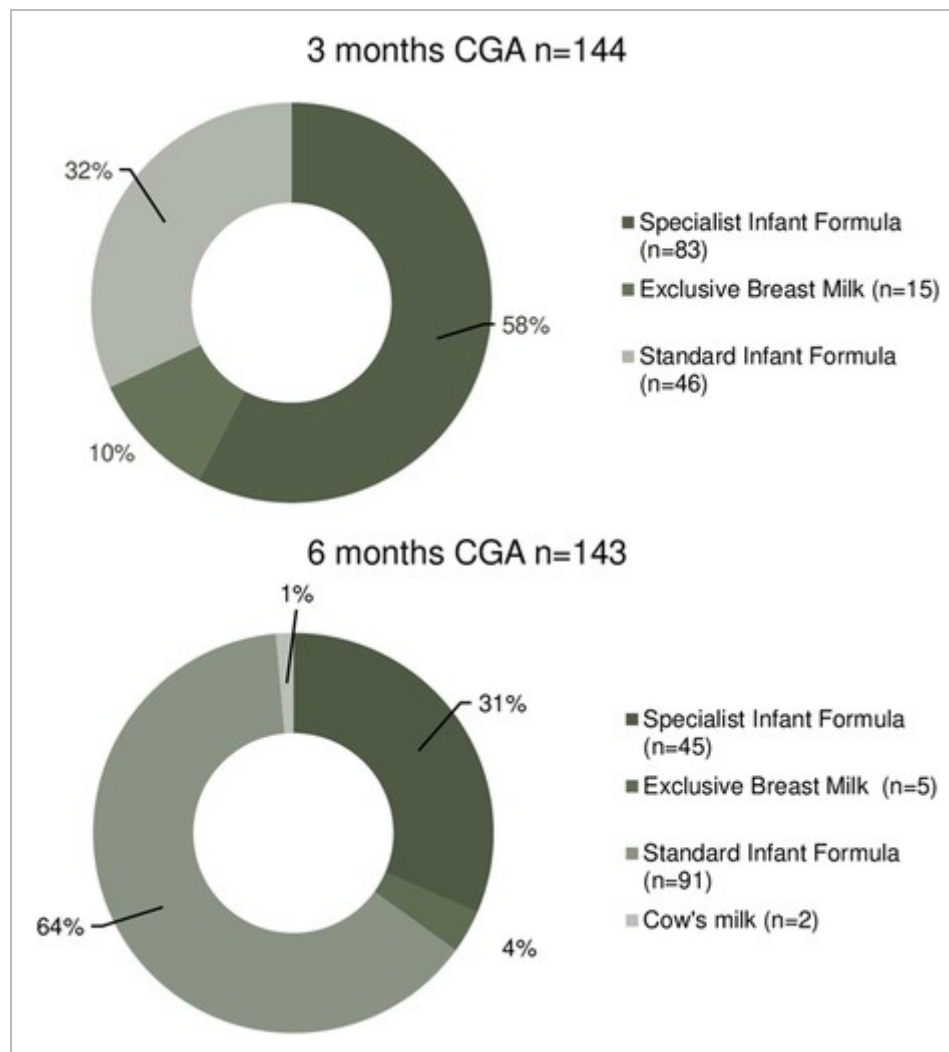


Figure 2

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Formula and breast milk use at 3 and 6 months corrected gestational age (CGA)

In total, 14 different formulas were used and 58% ($n = 83$) were using specialist milks (includes eHF/AA, preterm post-discharge formula, high energy, soya-based formulas). Two infants had a diagnosis of CMPA (1.4%) and were using an AA formula. Two remained on an eHF because of a background NEC, whereas one child with abnormal neurodevelopment was treated with an eHF for reflux and irritability.

All infants on eHF/AA formula ($n = 4$) were attending a dietician; in total, 27 (18.9%) of all infants included were attending a dietician 6 months CGA. One infant who had previously used eHF secondary to NEC had transitioned from eHF to standard infant formula. One hundred and seventeen infants (81.8%) had been documented as having commenced solid food. At 6 months CGA, 31.5% ($n = 45$) of ex premature infants remained on specialist formula, of which 60% were receiving preterm post discharge formula (Figure 2).

Two infants were already receiving standard cow's milk formula; however, they were 9 and 10 months CGA at the time of their 6-month review.

It was noted that infants who were receiving exclusive breast milk at discharge, were significantly more likely to still be receiving any breast milk at 3 ($p \leq 0.001$) and 6 months ($p \leq 0.001$) CGA compared to those combined feeding or exclusively formula feeding at discharge.

DISCUSSION

This report is the first Irish study to establish the prevalence of CMPA in preterm and/or VLBW infants.

Premature infants have increased gut permeability as a result of immature epithelial cells, and hence it was theorised that they were predisposed to early sensitisation and allergen development.²² VLBW infants were also considered to be at increased risk of allergy development secondary to reduced secretory IgA function, resulting in increased dietary antigen uptake.²³ However, a large population-based study of over 13,000 children found prematurity and low birth weight did not increase the development of IgE mediated food allergy.¹⁷ Similarly, a Norwegian study looked at the incidence of both IgE and non-IgE mediated CMPA in their infant population found no difference between ex premature and term infants in frequency, variety of symptoms or age at presentation. They included infants from 28 weeks of gestational age onwards.²⁴

Our findings are similar. We did not find any increase in the prevalence of CMPA in ex premature infants compared to the previously demonstrated prevalence in the general paediatric population. In our review, both infants with CMPA received a diagnosis following a clinical history descriptive of non-IgE mediated symptomatology, presented by 3 months CGA and showed improvement with dietary elimination. No cases were identified prior to discharge from the NICU. It is postulated that premature infants require T helper 2 cell adaptive immune maturation for the development of allergic symptoms, which occurs between 30 and 32 weeks of age, and may account for delayed presentation until after this time.²⁵

However, challenges remain in the recognition and diagnosis of CMPA in the preterm infant.⁸

Among a myriad of issues relating to prematurity, VLBW infants are at high risk of gastrointestinal complications including NEC and feed intolerances. The global incidence of NEC is 7% in VLBW infants.²⁶ CMPA and NEC may be difficult to distinguish clinically. NEC, similar to CMPA, only occurs after infants have been fed enterally. Cordova et al.⁸ suggested persistent feed intolerance post NEC or NEC-like illnesses should prompt clinicians to consider cow's milk intolerance in the preterm subgroup.

Premature infants who receive breast milk have a lower incidence of NEC than those who receive formula milk.²⁷ When breast milk is not available, alternatives such as eHF may be considered. A 2019 Cochrane review found that, when compared with standard formula use, eHFs did not affect the risk of feeding intolerance or NEC and therefore it was concluded that there was insufficient evidence to recommend their routine use.²⁸

In our review, both infants diagnosed with CMPA presented with symptoms to the outpatient department. Clinicians, general practitioners, public health nurses and all healthcare staff who may interact with premature infants following discharge should remain cognisant of CMPA, to ensure early recognition and management.

For the premature infant, human milk provides a vast array of substantial health benefits, both in the immediate aftermath following delivery and into adulthood. Advantages include decreased rates of NEC,²⁹ retinopathy of prematurity,³⁰ late onset sepsis³¹ and shortened hospitalisation time.³² Moving towards childhood and adult life, improved cardiovascular health and neurodevelopmental outcomes have been attributed to sustained use of human milk in the premature cohort.^{33, 34}

The World Health Organisation and UNICEF recommend exclusive breast-feeding for the first 6 months of life.³⁵ Ireland's breast-feeding rates are low. Only 37% of Irish neonates are exclusively receiving breast milk prior to discharge from hospital. This value does not differentiate between term and preterm cohorts. At 6 months 15% of term infants are exclusively breast-feeding in Ireland compared to a global average of 38% and European average of 25%.²⁰

In our cohort of very preterm and VLBW neonates, we found similar results upon discharge, with one-third receiving exclusive breast milk and a further 29% receiving combined feeding. However, at 6 months CGA, only 9% in our cohort of premature infants were receiving any breast milk. At 6 months CGA, almost 1 in 5 (18.9%) were attending a dietician. Over 30% were using specialist formula. Ideally, these infants using specialist formula should be linked with a paediatric dietician and undergo appropriate monitoring of growth and feeding.

We found that there was statistically significant increased chance of receiving any breast milk at 3 and 6 months CGA if discharged from the NICU exclusively receiving breast milk compared to formula or combined fed premature infants. It is imperative that breast feeding promotion, education, and a culture of support and partnership is established in the NICU prior to discharge. Moreover, following discharge, on-going breast-feeding support is

essential to ensure these infants continue to receive the benefits of breast milk as they grow.

An integral part of the breastfeeding education and maternal–child team is an International Board Lactation Consultant (IBCLC). Provision of full-time lactation support dedicated to NICU and high-risk preterm infants is shown to be associated with increased breastfeeding outcomes.³⁶ The US Lactation Consultants Association described optimal IBCLC staffing levels as 1.9 full time equivalents per 1000 deliveries in a tertiary maternity hospital.³⁷ In 2016, across Irish maternity hospitals, there was 13.2 whole time equivalent IBCLC posts and 62,039 births.³⁸ Applying this information and using gap analysis with the US Lactation Consultants recommendation as a benchmark, 110 whole time equivalent IBCLCs are required in Irish Maternity hospitals to reach the defined ideal staffing requirements.³⁸ Although these values convey the need for further dedicated posts to lactation support, it is also essential that all community health care staff interacting with new parents feel equipped to provide support, practical advice and empowerment to lactating mothers, encouraging sustained breast-feeding rates in the community, particularly in ex premature infants.

There were several limitations and caveats to our study. We conducted a single centre retrospective review with relatively small sample size of 144 patients. Diagnosis of non-IgE mediated CMPA in the clinical setting remains a challenge. We did not account for variables that may be confounding factors such as family history of atopy, maternal age, method of delivery and how growth velocity during NICU stay may have affected chosen type of feed.

In conclusion, the prevalence of CMPA in this very preterm and/or VLBW cohort was similar to the previously determined prevalence in the general paediatric population.

Although CMPA does not cause a large burden of disease in this cohort, we have highlighted the need for accessible dietetic services, both in-patient and post-discharge, for this population given the high prevalence of specialist formula use during the first year of life.

Sustained breastfeeding rates were lower in the ex preterm cohort compared to term infants in Ireland, despite the known benefits of breast milk. This strongly conveys the importance of education, optimisation and promotion of breastfeeding in the NICU by all healthcare professionals. Access to lactation consultants is required antenatally, postnatally and post-discharge from hospital to sustain breastfeeding in this vulnerable population. Public health initiatives focusing on breast milk for the premature infant are warranted with additional concentration on provision of accessible community supports once discharged home.

Larger, prospective studies are warranted eliciting the role of prematurity and delineating possible contributing factors such as NEC, growth, feed type and familial predisposition in the development of CMPA.

CONFLICT OF INTERESTS

The authors declare that there are no conflicts of interest.

ETHICAL APPROVAL

Ethical approval was sought and obtained prior to commencing this study. The Rotunda Hospital Research and Ethics Committee granted approval for this retrospective study (approval number 2020-034).

AUTHOR CONTRIBUTIONS

Davina Henderson was lead author. Roles included literature review, data collection and drafting the initial manuscript. Claire A. Murphy contributed to study design, acquisition of data, statistical analysis of the data and writing of the final manuscript. Anna-Claire Glynn's role included contribution to methodology, expertise in Neonatal Dietetics, editing and revision of manuscript. Michael A. Boyle provided project design and clinical advice, data interpretation and revision of the manuscript. Naomi McCallion's roles included conceptualisation of the work, supervision, advice and critique of the manuscript. All authors reviewed and approved the final manuscript submitted for submission.

TRANSPARENCY DECLARATION

The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained.

Biographies

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REFERENCES



1 Lifschitz C, Szajewska H. Cow's milk allergy: evidence-based diagnosis and management for the practitioner. *Eur J Pediatr*. 2015; **174**(2): 141– 50.

[Crossref](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

2 Schoemaker AA, Sprickelman AB, Grimshaw KE. Incidence and natural history of challenge-proven cow's milk allergy in European children–EuroPrevall birth cohort. *Allergy*. 2015; **70**(8): 963–72. <https://doi-org.bibliosan.clas.cineca.it/10.1111/all.12630>

[Wiley Online Library](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

3 Ludman S, Shah N, Fox AT. Managing cows' milk allergy in children. *Br Med J*. 2013; **347**:f5424.

[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

4 Sicherer SH. Epidemiology of food allergy. *J Allergy Clin Immunol*. 2011; **127**(3): 594– 602.

<https://doi-org.bibliosan.clas.cineca.it/10.1016/j.jaci.2010.11.044>

[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

5 Høst A. Frequency of cow's milk allergy in childhood. *Ann Allergy Asthma Immunol*. 2002; **89**(6 Suppl 1): 33– 7.

[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

6 Sladkevicius E, Nagy E, Lack G, Guest JF. Resource implications and budget impact of managing cow milk allergy in the UK. *J Med Econ*. 2010; **13**(1): 119– 28.

[Crossref](#) | [CAS](#) | [PubMed](#) | [Google Scholar](#)

7 Koletzko S, Niggemann B, Arato A, Dias JA, Heuschkel R, Husby S, et al. Diagnostic approach and management of cow's-milk protein allergy in infants and children: ESPGHAN GI Committee Practical Guidelines. *J Pediatr Gastroenterol Nutr*. 2012; **55**(2): 221– 9.

[Crossref](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

8 Cordova J, Sriram S, Patton T, Jericho H, Gokhale R, Weinstein D, et al. Manifestations of cow's-milk protein intolerance in preterm infants. *J Pediatr Gastroenterol Nutr*. 2016; **62**(1): 140– 4.

[Crossref](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

9 Healthcare Pricing Office (HPO), Health Service Executive (HSE) Perinatal Statistics Report. 2016.

[Google Scholar](#)

10 Leitao S, Corcoran, P, Twomey A, Murphy BP, Greene RA. on behalf of NICORE Republic of Ireland (2020) Very Low Birth Weight Infants in the Republic of Ireland Annual Report 2018, Cork: National Perinatal Epidemiology Centre

[Google Scholar](#)

-
- 11 Hay WW Jr. Nutritional support strategies for the preterm infant in the neonatal intensive care unit. *Pediatr Gastroenterol Hepatol Nutr*. 2018; **21**(4): 234– 47.
[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)
-
- 12 Victora CG, Bahl R, Barros AJ, França GV, Horton S, Krasevec J, et al. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. *Lancet*. 2016; **387**(10017): 475– 90.
[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)
-
- 13 Arslanoglu S, Boquien C-Y, King C, Lamireau D, Tonetto P, Barnett D, et al. Fortification of human milk for preterm infants: Update and recommendations of the European Milk Bank Association (EMBA) Working Group on Human Milk Fortification. *Front Pediatr*. 2019; **7**: 76.
[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)
-
- 14 Kelly E, DunnGalvin G, Murphy BP, O'B Hourihane J. Formula supplementation remains a risk for cow's milk allergy in breast-fed infants. *Pediatr Allergy Immunol*. 2019; **30**(8): 810– 6.
[Wiley Online Library](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)
-
- 15 Zachariassen G, Faerk J, Esberg BH, Fenger-Gron J, Mortensen S, Christesen HT, et al. Allergic diseases among very preterm infants according to nutrition after hospital discharge. *Pediatr Allergy Immunol*. 2011; **22**(5): 515– 20.
[Wiley Online Library](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)
-
- 16 Chiale F, Maggiora E, Aceti A, Liotto N, Coscia A, Peila C, et al. Complementary feeding: recommendations for the introduction of allergenic foods and gluten in the preterm infant. *Nutrients*. 2021; **13**: 7.
[Crossref](#) | [Web of Science®](#) | [Google Scholar](#)
-
- 17 Liem JJ, Kozyrskyj AL, Huq SI, Becker AB. The risk of developing food allergy in premature or low-birth-weight children. *J Allergy Clin Immunol*. 2007; **119**(5): 1203– 9.
[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)
-
- 18 Siltanen M, Wehkalampi K, Hovi P, Eriksson JG, Strang-Karlsson S, Järvenpää AL, et al. Preterm birth reduces the incidence of atopy in adulthood. *J Allergy Clin Immunol*. 2011; **127**(4): 935– 42.
[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)
-
- 19 Reynolds A, O'Driscoll J, Quinn S, Coughlan D. Cows milk allergy: a cohort of patients from a university hospital. *Ir Med J*. 2016; **109**(4): 390.
[CAS](#) | [PubMed](#) | [Google Scholar](#)
-
- 20 National Women and Infants and Health Programme (HSE). Irish Maternity Indicator System. HAE; 2019: October 2020; 2019 [cited Feb 2021].
[Google Scholar](#)
-
- 21 Venter C, Brown T, Meyer R, Walsh J, Shah N, Nowak-Węgrzyn A, et al. Better recognition, diagnosis and management of non-IgE-mediated cow's milk allergy in infancy: iMAP—an

international interpretation of the MAP (Milk Allergy in Primary Care) guideline. *Clin Transl Allergy*. 2017; **7**: 26.

[Wiley Online Library](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

22 Roberton DM, Paganelli R, Dinwiddie R, Levinsky RJ. Milk antigen absorption in the preterm and term neonate. *Arch Dis Child*. 1982; **57**(5): 369–72.

[Crossref](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

23 Taylor B, Norman AP, Orgel HA, Stokes CR, Turner MW, Soothill JF. Transient IgA deficiency and pathogenesis of infantile atopy. *Lancet*. 1973; **2**(7821): 111–3.

[Crossref](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

24 Kvenshagen B, Halvorsen R, Jacobsen M. Adverse reactions to milk in infants. *Acta Paediatr*. 2008; **97**(2): 196–200.

[Wiley Online Library](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

25 Morita Y, Iwakura H, Ohtsuka H, Kohno Y, Shimojo N. Milk allergy in the neonatal intensive care unit: comparison between premature and full-term neonates. *Asia Pac Allergy*. 2013; **3**(1): 35–41.

[Crossref](#) | [PubMed](#) | [Google Scholar](#)

26 Alsaied A, Islam N, Thalib L. Global incidence of Necrotizing Enterocolitis: a systematic review and meta-analysis. *BMC Pediatr*. 2020; **20**(1): 344.

[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

27 Altobelli E, Angeletti PM, Verrotti A, Petrocelli R. the impact of human milk on necrotizing enterocolitis: a systematic review and meta-analysis. *Nutrients*. 2020; **12**: 5.

[Crossref](#) | [Google Scholar](#)

28 Ng DHC, Klassen JR, Embleton ND, McGuire W. Protein hydrolysate versus standard formula for preterm infants. *Cochrane Database Syst Rev*. 2019; **7**(7):Cd012412.

[PubMed](#) | [Google Scholar](#)

29 Sisk PM, Lovelady CA, Dillard RG, Gruber KJ, O'Shea TM. Early human milk feeding is associated with a lower risk of necrotizing enterocolitis in very low birth weight infants. *J Perinatol*. 2007; **27**(7): 428–33.

[Crossref](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

30 Okamoto T, Shirai M, Kokubo M, Takahashi S, Kajino M, Takase M, et al. Human milk reduces the risk of retinal detachment in extremely low-birthweight infants. *Pediatr Int*. 2007; **49**(6): 894–7.

[Wiley Online Library](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

31 Schanler RJ, Shulman RJ, Lau C. Feeding strategies for premature infants: beneficial outcomes of feeding fortified human milk versus preterm formula. *Pediatrics*. 1999; **103**(6 Pt 1): 1150–7.

[Crossref](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

32 Healy DB, Brennan AM, O'Donovan R, Daly V, Doolan A, Dempsey EM. Structured promotion of breastmilk expression is associated with shortened hospitalisation for very preterm infants. *Acta Paediatr.* 2016; **105**(6): e252–6.

[Wiley Online Library](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

33 El-Khuffash A, Jain A, Lewandowski AJ, Levy PT. Preventing disease in the 21st century: early breast milk exposure and later cardiovascular health in premature infants. *Pediatr Res.* 2020; **87**(2): 385–90.

[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

34 Isaacs EB, Fischl BR, Quinn BT, Chong WK, Gadian DG, Lucas A. Impact of breast milk on intelligence quotient, brain size, and white matter development. *Pediatr Res.* 2010; **67**(4): 357–62.

[Crossref](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

35 World Health Organisation. Breastfeeding recommendations [cited March 2020]. Available from: <https://www.who.int/health-topics/breastfeeding>

[Google Scholar](#)

36 Gharib S, Fletcher M, Tucker R, Vohr B, Lechner BE. Effect of dedicated lactation support services on breastfeeding outcomes in extremely-low-birth-weight neonates. *J Hum Lact.* 2018; **34**(4): 728–36.

[PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

37 Walker M. *Feeding management for the clinician: Using the evidence*. 4th ed. MA: Jones and Bartlett; 2016.

[Google Scholar](#)

38 HSE National Breastfeeding Implementation Group. Report of the review of breastfeeding resources in Maternity Hospitals/Units and Community Health Organisations. 2017.

[Google Scholar](#)

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