Demographic profile, food trigger associations and trends in outcome of infants with food protein-induced enterocolitis syndrome: a single tertiary centre Australian cohort study

Eric Lee[1], Elizabeth Barnes[2], Sam Mehr[3], and Dianne Campbell[2]

[1]The University of Sydney
[2]University of Sydney
[3]Children's Hospital at Westmead

October 1, 2020

Abstract

Background: Food protein-induced enterocolitis syndrome (FPIES) is a non-IgE mediated food allergic disorder with a well-characterised clinical phenotype, but limited understanding of factors associated with food cross-reactivity, severity and tolerance. Methods: A retrospective cohort study spanning 20 years on children with acute FPIES from a single paediatric tertiary centre in New South Wales, Australia focusing on identifying food trigger co-associations and factors associated with reaction severity, multiple trigger FPIES and/or tolerance was performed. Results: 169 individuals with 329 recorded FPIES episodes between 1997 and 2017 were included. 49% were male. The median age at first FPIES reaction was 5 months and median age at diagnosis was 9 months. 73% experienced at least one severe FPIES reaction. Rice (45%), cow's milk (30%), soy (13%) were the most common triggers. FPIES to rice or cow's milk were strongly associated with increased odds of having multiple trigger FPIES. Associations between causative foods were seen with rice/oats, cow's milk/soy, and fish/shellfish. No factors were associated with increased risk of severe reactions. Infants with rice and grains FPIES outgrew their reactions at an earlier age, compared to those with fish FPIES. Conclusions: Background: Food protein-induced enterocolitis syndrome (FPIES) is a non-IgE mediated food allergic disorder with a well-characterised clinical phenotype, but limited understanding of factors associated with food cross-reactivity, severity and tolerance. Methods: A retrospective cohort study spanning 20 years on children with acute FPIES from a single paediatric tertiary centre in New South Wales, Australia focusing on identifying food trigger co-associations and factors associated with reaction severity, multiple trigger FPIES and/or tolerance was performed. Results: 169 individuals with 329 recorded FPIES episodes between 1997 and 2017 were included. 49% were male. The median age at first FPIES reaction was 5 months and median age at diagnosis was 9 months. 73% experienced at least one severe FPIES reaction. Rice (45%), cow's milk (30%), soy (13%) were the most common triggers. FPIES to rice or cow's milk were strongly associated with increased odds of having multiple trigger FPIES. The odds of having multiple food FPIES and severe reactions were slightly decreased with vaginal delivery. No factors were associated with increased risk of severe reactions. Infants with rice and grains FPIES outgrew their reactions at an earlier age, compared to those with fish FPIES. Conclusions: Rice remains the most common trigger for FPIES in this region with co-associations between rice/oats and cow's milk/soy observed. The co-associations among food groups suggest that taxonomically related foods share similar protein structure and trigger similar mechanisms of antigen recognition. Vaginal delivery appears to have a mild protective effect on the development of multiple FPIES and severe reactions.

Demographic profile, food trigger associations and trends in outcome of infants with food protein-induced enterocolitis syndrome: a single tertiary centre Australian cohort study

E Lee[1,2], EH Barnes[3], S Mehr[2], DE Campbell[1,2]

[1], Discipline of Child and Adolescent Health, Faculty of Medicine and Health, The University of Sydney

[2] Department of Allergy and Immunology, The Children's Hospital at Westmead, Sydney, NSW

[3] NHMRC Clinical Trials Centre, Faculty of Medicine and Health, The University of Sydney

*The authors declare that there are no conflicts of interest.

Word count: 3364 (not including abstract)

Abstract

Background:

Food protein-induced enterocolitis syndrome (FPIES) is a non-IgE mediated food allergic disorder with a well-characterised clinical phenotype, but limited understanding of factors associated with food cross-reactivity, severity and tolerance.

Methods:

A retrospective cohort study spanning 20 years on children with acute FPIES from a single paediatric tertiary centre in New South Wales, Australia focusing on identifying food trigger co-associations and factors associated with reaction severity, multiple trigger FPIES and/or tolerance was performed.

Results:

169 individuals with 329 recorded FPIES episodes between 1997 and 2017 were included. 49% were male. The median age at first FPIES reaction was 5 months and median age at diagnosis was 9 months. 73% experienced at least one severe FPIES reaction. Rice (45%), cow's milk (30%), soy (13%) were the most common triggers. FPIES to rice or cow's milk were strongly associated with increased odds of having multiple trigger FPIES. The odds of having multiple food FPIES and severe reactions were slightly decreased with vaginal delivery. No factors were associated with increased risk of severe reactions. Infants with rice and grains FPIES outgrew their reactions at an earlier age, compared to those with fish FPIES.

Conclusions:

Rice remains the most common trigger for FPIES in this region with co-associations between rice/oats and cow's milk/soy observed. The co-associations among food groups suggest that taxonomically related foods share similar protein structure and trigger similar mechanisms of antigen recognition. Vaginal delivery appears to have a mild protective effect on the development of multiple FPIES and severe reactions.

Key statement

Regional variations in the clinical phenotype of FPIES exist, with consistent trends seen in Australian children. Although no significant predictive factors influence the prognostic outcomes in FPIES, the clinical implications of our findings allow evidence-based management and advice provided for parents of children with FPIES.

Introduction

Food protein-induced enterocolitis syndrome (FPIES) is a non-IgE mediated food allergic disorder predominantly affecting infants and children. Despite a poor understand of the pathophysiology of FPIES, several large clinical cohorts have been published, and international consensus guidelines for the diagnosis have been established[1].

We previously performed a prospective population-based study across Australia examining the incidence, clinical characteristics and food trigger associations for infants with FPIES [2]. This demonstrated an incidence of 15.4/100,000/year in infants less than 2 years of age, suggesting that FPIES is more common than previously recognised. Other studies have demonstrated higher rates of FPIES, with Katz et al. demonstrating a cumulative incidence of 0.34% of cow's milk FPIES in an Israeli cohort [3], and Alonso et al. demonstrating an incidence of 0.7% in a Spanish cohort[4].

There is a recognised regional variation in the causative food triggers associated with FPIES, with cow's milk, soy, rice and fish being the most common triggers [3, 5, 6]. Australia is the only region to have consistently reported rice as the most common cause of FPIES. Fish FPIES is common in southern Europe, whilst most US and UK studies report cow's milk as the most common trigger [5, 7, 8].

Here, we sought to determine the consistency of identified trends in Australian patients with FPIES by characterising the demographic profile, medical history and food trigger associations of a single tertiary centre cohort of patients collected over a 20-year period. We sought to identify risk factors associated with co-associations, severity of reaction and resolution of FPIES.

Methods

Patient identification

Patients were initially identified from a database in the Allergy Department at the Children's Hospital at Westmead (CHW), New South Wales (NSW), Australia [9], consisting of children with FPIES aged between 1 months and 6 years at the time of diagnosis, presenting for management between 1997 and 2017. Patients were screened for inclusion based upon modified criteria from international consensus guidelines outlined by Nowak et al. [1] (Table 1), limited to those meeting the major and 3 or more minor criteria.

Data collection and analysis

Data were obtained from retrospective review of the medical records repository. Birth history, feeding history and personal and family history of atopic comorbidities were recorded. Outcomes of single versus multiple ([?] 2 individual food triggers), severe FPIES reactions (presence of vomiting and accompanying symptoms of floppiness, lethargy and pallor), and resolution of FPIES based on results of an in-hospital oral food challenge where available were recorded.

Statistical analysis

Predictors of developing severe FPIES reactions and multiple trigger FPIES were explored using logistic regression with odds ratio (OR) estimates and 95% confidence intervals (CI) presented. Age at resolution of FPIES was described using the Kaplan-Meier method and predictors tested using proportional hazards regression models, with hazard ratios (HR) and CI presented. Pearson correlation coefficients were used to examine correlations among individual food triggers. Analysis was performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC) and GraphPad Prism 8 (GraphPad Software, La Jolla, Calif).

Ethics

Ethics approval was granted by the Sydney Children's Hospitals Network Human Research Ethics Committee (2019/ETH11529).

Results

Overview

169 individuals with 329 episodes of FPIES met inclusion criteria. Their demographic characteristics are displayed in Table 2. 29/169 were participants of the population-wide prospective cohort study in 2015[10].

Birth history

Birth and gestation data were available in 108 and 112 children respectively (Table 2). The median gestational age was 40 weeks (interquartile range (IQR)=38-40) and the mean birthweight was 3270g (standard deviation (SD)=570). Six children had low birthweight (less than 2500g), four of whom were premature, and the youngest born at 30 weeks' gestation.

Feeding history

Data regarding breastfeeding history was available for 134/169 (79%) children. 130 children (97%) were breastfed, with a median breastfeeding duration of 7 months (IQR=6-10). Information regarding exclusive

breastfeeding in the first 4 months was available in 122 infants, 79 of whom were exclusively breastfed to at least 4 months of age. Only 4 children were exclusively formula-fed from birth. The median age when solids were first introduced was 5 months (IQR=4.5-6). The most common weaning foods were rice (75/94); fruit (52/94) (apple, pear, avocado and banana); and vegetables (52/94) (carrots, sweet potato and pumpkin).

Personal history, family history and comorbid atopy

All patients were fully immunised by 12 months of age as per the Australian National Immunisation Program Schedule [11]. 53% of children had comorbid atopy (Table 2). IgE-mediated food allergy was common (n=32, 19%) based on a clinical history of a reaction and positive skin prick test or serum specific IgE to the food trigger. Egg (17/32) and cow's milk (11/32) were the most common triggers for IgE-mediated food allergy. The prevalence of family history of FPIES and atopy are shown in Table 2. Atopy was present in similar proportions in the child's mother (25/89), father (28/89) or siblings (27/89).

Food triggers

The most common food triggers were rice (45%), cow's milk (30%), soy (13%) and eggs (12%) (Table 2). multiple FPIES occurred in 36% individuals. No factors from were strongly associated with developing multiple FPIES (Figure 1). There was no association between FPIES to multiple triggers and vaginal delivery versus caesarean section (OR=.68, CI=0.3-1.6, P =0.36). There were slightly higher odds of having FPIES to multiple triggers with increased breastfeeding duration (OR=1.1 per month, CI=1-1.2, P =0.03).

Rice (OR=3.7, CI=1.9-7.2, P <.001) and cow's milk (OR=3.2, CI=1.6-6.4, P <0.001) were associated with increased odds of having FPIES to multiple food triggers. By phi coefficient, there was correlation between rice and oats; eggs and other grains; cow's milk and soy; and fish and shellfish as a trigger, but most correlations were low (Figure 2). Of 39 children with rice FPIES who had multiple food trigger, 16 (41%) were reactive to oats, 13 (33%) reacted to fruits and vegetables, 12 (31%) reacted to cow's milk, and 5 (13%) reacted to eggs. 28 children with milk FPIES had multiple food triggers, 12 (43%) who also reacted to soy, 12 reacting to fruits and vegetables, and 5 (18%) reacting to eggs.

Associations with severity of FPIES reactions

123 children (73%) experienced at least one severe FPIES reaction, having all 3 cardinal features of FPIES (vomiting with lethargy, floppiness and pallor). All 40 infants requiring IV fluid administration met criteria for a severe reaction. Vaginal delivery (OR=0.4, CI=0.2-1.2, P =0.097) and an increased duration of breastfeeding (OR=0.9 per month, CI=0.8-1.0, P =0.05) appeared to be negatively associated with experiencing a severe FPIES reaction. No particular food group or other factors were associated with an increased risk of a severe FPIES reaction (Figure 1).

Associations with acquisition of tolerance

Over the study duration, there were records from 88/169 children who underwent formal oral food challenge for their FPIES triggers. 67 of these children did not react at time of food challenge. The median age for acquisition of tolerance was 25 months (IQR=20-35). Infants who had their first FPIES reaction at a later age were more likely to acquire tolerance at a later age (HR=0.95 per month, CI=0.91-0.99,P= 0.02) (Figure 3). Children with FPIES to rice and other grains were likely to acquire tolerance at an earlier age (HR=1.9, CI=1.2-3.2,P =.0099) whilst children with FPIES to fish were likely to acquire tolerance at a later age (HR 0.2, CI=0.08-0.6, P =.0039) (Figure 4). No other factors affected age of tolerance acquisition (Figure 3).

Discussion

The clinical phenotype of FPIES is well described, with several large-scale retrospective cohort studies published over the last two decades. Despite this, the reason why there are prominent geographic variations in types of food triggers, rates of multiple food FPIES and why children outgrow FPIES remain unknown. Regional breastfeeding and weaning practices have been proposed to influence these factors.

We have previously investigated the impact of infant feeding practices on the development of FPIES to

multiple triggers, in addition to the associations among different food groups in infants with multiple food FPIES [2]. Rice was the most common food trigger in Australian children, with 32% of the total cohort having FPIES to multiple food triggers. Here, we demonstrate that rice is consistently the most common trigger in Australian infants (in 45%). This is in contrast to other regions with cow's milk being the most common in the United Kingdom, USA and Israel, and with fish being a predominant solid food trigger in Italy and Spain [3, 5, 6, 8, 12]. Only one other study outside of Australia, in the USA, identified rice as more frequent a trigger than cow's milk [13]. Interestingly, in our cohort, infants with rice FPIES were unlikely to react to cow's milk or fish but were more likely to have FPIES to multiple foods.

We identified a rate of FPIES to multiple food triggers within the whole cohort of 36% in keeping with previous Australian data[2], and in comparison with other countries, highest in the USA (up to 50%) and United Kingdom (30%) [5, 14], and lowest in Spain (16%) and Italy (15%) [6, 15]. Here we demonstrate a possible trend towards increased risk of FPIES to multiple triggers in children who were delivered via caesarean section. The mode of delivery has long been proposed to impact upon the development of food allergy and atopy [16], with delivery via caesarean section thought to disrupt the maternal transference of microbiota to the infant. Katz et al. reported a higher prevalence of delivery via caesarean section in infants with cow's milk FPIES, two times compared to vaginal delivery [3].

Our previous population-based study demonstrated that duration of exclusive breastfeeding less than four months was associated with increased risk of multiple food FPIES (11% versus 20%)[2]. This was not seen within this study's cohort. Instead, there was a weak association between increased duration of breastfeeding and increased risk of multiple food FPIES. It may be that mothers of children who have experienced multiple FPIES may choose to breastfeed for longer duration, due to the perceived relative safety of breastfeeding in triggering an FPIES reaction, thus a potential for reverse causation. Few studies have examined infant feeding practices in association with FPIES, and those which have, demonstrate similar or mildly higher rates of FPIES in infants who are not breastfed, or have shorter duration of breastfeeding [5, 6]. Overall the rate of breastfeeding in this population is high, compared to other countries with well documented FPIES cohorts. Feeding practices and their impact on FPIES development and phenotype warrant further prospective investigation.

Co-associations between food triggers in children with multiple FPIES were observed between rice and oats; cow's milk and soy; and fish and shellfish, consistent with previous data in reported case series[17]. We observed a co-association between eggs and other grains (which included wheat and rye) in our cohort not previously documented in other reports. Cow's milk/soy cross-reactivity is commonly seen in US populations (up to 50% in case series), as is rice/oats cross-reactivity (up to 30%) in US and Australia [1]. Although fish and shellfish FPIES are more prevalent in Mediterranean countries, the reported rates of cross-reactivity are similar[18]. Children with rice and cow's milk FPIES had an increased risk of FPIES to multiple foods. This may be due to rice and cow's milk being the most common food triggers within the cohort, in addition to the higher prevalence of co-association between rice/oats and cow's milk/soy.

Atopy in siblings was another risk factor for multiple FPIES with a 1.6-fold risk. In contrast, a family history of FPIES was rare and not associated with increased risk of multiple FPIES, although the numbers for this analysis were small. This is similar to previous epidemiological data demonstrating low familial risk of FPIES[19]. Both a family and personal history of atopy is common in Australian infants and although not examined in local populations, a US study has reported a higher rate of comorbid atopy in infants with FPIES compared to healthy infants [20]. In our cohort, eczema was the most common comorbid atopy and was strongly associated with IgE-mediated food allergy, particularly to eggs, similarly demonstrated by Ruffner et al. [20]. Additionally, there is a risk of conversion from FPIES to IgE food allergy, especially with cow's milk FPIES [1]. It would be of interest to conduct a longitudinal study to observe for the rates of development of IgE food allergy, given the apparent existing high background risk.

Proposed definitions for severity of FPIES reactions have been characterised by international guidelines [1], and few descriptive case series have observed potential increased severity in association with solid food triggers, however reports are varying. In our cohort, the rate of experiencing at least one severe reaction was

high, at nearly 75% of the cohort, however no risk factors for severity were identified.

We have previously reported variations in timing to acquisition of tolerance to different causative food triggers [21]. Fifty five of 169 infants were participants in this previous study[21]. Here, we demonstrate similar findings of earlier resolution for rice FPIES but delayed resolution for fish FPIES. Infants who had their first reaction at a later age attained tolerance at a later age, likely related to the sequence of exposure to different solid foods. Although we did not find any predictive factors of tolerance from feeding history, Sopo et al. demonstrated that earlier tolerance acquisition in FPIES to eggs was achieved by the effect of cooking[22], providing potential insight into how food protein interactions with immune mechanisms may dictate responses. Despite a proof of tolerance via supervised oral food challenge (OFC), a recent study by Argiz et al. reported reactions upon re-exposure to trigger foods following a negative OFC in 13% of infants, most likely to occur with egg and fish FPIES [23]. These findings aid in recommendations for feeding practices and first weaning foods for infants with FPIES.

Our study is limited by the retrospective nature, which is prone to recall bias. In addition, our sample size is limited by selection of a group of individuals known to a tertiary specialised centre, with possible identification of a more severe cohort of patients with FPIES, as illustrated by the high proportion of subjects who experienced at least one severe episode. Missing data on mode of birth, and incomplete feeding histories limit the conclusions which can be drawn about these analyses.

Our findings over 20 years of children with FPIES managed at a large single centre demonstrate many similarities with the published population-based survey of Australian infants with FPIES, which examined only FPIES presentations from 2012-14. Notably, we observed decreased odds of the development of multiple food FPIES and severe reactions in infants who were born via vaginal delivery, and a possible variable effect of breastfeeding, with longer duration of breastfeeding seen in infants with multiple food FPIES, but with a decreased risk of development of severe reactions. Important clinical implications include identifying that infants presenting with cow's milk or rice FPIES may be at greatest risk of the development of FPIES to other foods and that severity of FPIES reactions appears not to be readily predictable by food trigger or other baseline characteristics.

References

1. Nowak-Węgrzyn A, Chehade M, Groetch ME, Spergel JM, Wood RA, Allen K, et al. International consensus guidelines for the diagnosis and management of food protein–induced enterocolitis syndrome: Executive summary—Workgroup Report of the Adverse Reactions to Foods Committee, American Academy of Allergy, Asthma & Immunology. Journal of Allergy and Clinical Immunology 2017; 139:1111-26.e4.

2. Mehr S, Frith K, Barnes EH, Campbell DE. Food protein–induced enterocolitis syndrome in Australia: A population-based study, 2012-2014. Journal of Allergy and Clinical Immunology 2017.

3. Katz Y, Goldberg MR, Rajuan N, Cohen A, Leshno M. The prevalence and natural course of food protein-induced enterocolitis syndrome to cow's milk: a large-scale, prospective population-based study. Journal of Allergy and Clinical Immunology 2011; 127:647-53.e1-3.

4. Alonso SB, Ezquiaga JG, Berzal PT, Tardon SD, San Jose MM, Lopez PA, et al. Food protein-induced enterocolitis syndrome: Increased prevalence of this great unknown-results of the PREVALE study. Journal of Allergy and Clinical Immunology 2019; 143:430-3.

5. Ruffner MA, Ruymann K, Barni S, Cianferoni A, Brown-Whitehorn T, Spergel JM. Food protein-induced enterocolitis syndrome: insights from review of a large referral population. Journal of Allergy and Clinical Immunology in Practice 2013; 1:343-9.

6. Sopo SM, Giorgio V, Dello Iacono I, Novembre E, Mori F, Onesimo R. A multicentre retrospective study of 66 Italian children with food protein-induced enterocolitis syndrome: different management for different phenotypes. Clinical and Experimental Allergy 2012; 42:1257-65.

7. Leung PS, Shu SA, Chang C. The changing geoepidemiology of food allergies. Clinical Reviews in Allergy and Immunology 2014; 46:169-79.

8. Ludman S, Harmon M, Whiting D, du Toit G. Clinical presentation and referral characteristics of food protein-induced enterocolitis syndrome in the United Kingdom. Annals of Allergy, Asthma and Immunology 2014; 113:290-4.

9. Lee E, Barnes EH, Mehr S, Campbell DE. Differentiating Acute Food Protein-Induced Enterocolitis Syndrome From Its Mimics: A Comparison of Clinical Features and Routine Laboratory Biomarkers. Journal of Allergy and Clinical Immunology in Practice 2019; 7:471-8 e3.

10. Mehr SS, Campbell D, Joshi P, Smart J, Peake JE, Smith PK, et al. FPIES Epidemiology in Australia: Results from a 2-Year Prospective Population Study. Journal of Allergy and Clinical Immunology 2015; 135:AB168.

11. National Immunisation Program Schedule. Australian Government Department of Health. Last updated 19 March 2020. Available from https://www.health.gov.au/health-topics/immunisation/immunisation-throughout-life/national-immunisation-program-schedule.

12. Villafana L, Cepeda ST, Perez N, De La Hoz B, Alvarez-Cuesta E. Food Induced Gastroenterocolitis Syndrome(FPIES): A Case Series of 51 Children. Journal of Allergy and Clinical Immunology 2015; 135:AB47.

13. Blackman A, Anagnostou A. Triggers and Management of FPIES in a Pediatric US population. Journal of Allergy and Clinical Immunology 2019; 143.

14. Caubet JC, Ford LS, Sickles L, Jarvinen KM, Sicherer SH, Sampson HA, et al. Clinical features and resolution of food protein-induced enterocolitis syndrome: 10-year experience. Journal of Allergy and Clinical Immunology 2014; 134:382-9.

15. Diaz JJ, Espin B, Segarra O, Dominguez-Ortega G, Blasco-Alonso J, Cano B, et al. Food Protein-induced Enterocolitis Syndrome: Data From a Multicenter Retrospective Study in Spain. Journal of Pediatric Gastroenterology and Nutrition 2019; 68:232-6.

16. Mitselou N, Hallberg J, Stephansson O, Almqvist C, Melen E, Ludvigsson JF. Cesarean delivery, preterm birth, and risk of food allergy: Nationwide Swedish cohort study of more than 1 million children. Journal of Allergy and Clinical Immunology 2018; 142:1510-4 e2.

17. Infante S, Cabrera-Freitag P, Morales-Cabeza C, Alvarez-Perea A. Geographical Variations in Food Protein-Induced Enterocolitis Syndrome. Current Treatment Options in Allergy 2019:1-13.

18. Miceli Sopo S, Monaco S, Badina L, Barni S, Longo G, Novembre E, et al. Food protein-induced enterocolitis syndrome caused by fish and/or shellfish in Italy. Pediatric Allergy and Immunology 2015; 26:731-6.

19. Mehr S, Frith K, Campbell DE. Epidemiology of food protein-induced enterocolitis syndrome. Current Opinion in Allergy and Clinical Immunology 2014; 14:208-16.

20. Ruffner MA, Wang KY, Dudley JW, Cianferoni A, Grundmeier RW, Spergel JM, et al. Elevated Atopic Comorbidity in Patients with Food Protein–Induced Enterocolitis. Journal of Allergy and Clinical Immunology in Practice 2020; 8:1039-46.

21. Lee E, Campbell DE, Barnes EH, Mehr SS. Resolution of acute food protein-induced enterocolitis syndrome in children. Journal of Allergy and Clinical Immunology in Practice 2017; 5:486-8 e1.

22. Miceli Sopo S, Romano A, Bersani G, Fantacci C, Badina L, Longo G, et al. Cooking influence in tolerance acquisition in egg-induced acute food protein enterocolitis syndrome. Allergologia et Immunopathologia 2019; 47:221-6.

23. Argiz L, Infante S, Machinena A, Pascal M, Echeverria L, Barni S, et al. Reactions on re-exposure following negative and inconclusive follow-up food challenges in children with acute FPIES. Journal of Allergy and Clinical Immunology in Practice 2020.

Hosted file

`Table 1.pdf` available at https://authorea.com/users/362811/articles/483826-demographic-profile-food-trigger-associations-and-trends-in-outcome-of-infants-with-food-protein-induced-enterocolitis-syndrome-a-single-tertiary-centre-australian-cohort-study

Hosted file

`Table 2.pdf` available at https://authorea.com/users/362811/articles/483826-demographic-profile-food-trigger-associations-and-trends-in-outcome-of-infants-with-food-protein-induced-enterocolitis-syndrome-a-single-tertiary-centre-australian-cohort-study

Hosted file

`Figure 1.pdf` available at https://authorea.com/users/362811/articles/483826-demographic-profile-food-trigger-associations-and-trends-in-outcome-of-infants-with-food-protein-induced-enterocolitis-syndrome-a-single-tertiary-centre-australian-cohort-study

Hosted file

`Figure 2.pdf` available at https://authorea.com/users/362811/articles/483826-demographic-profile-food-trigger-associations-and-trends-in-outcome-of-infants-with-food-protein-induced-enterocolitis-syndrome-a-single-tertiary-centre-australian-cohort-study

Hosted file

`Figure 3.pdf` available at https://authorea.com/users/362811/articles/483826-demographic-profile-food-trigger-associations-and-trends-in-outcome-of-infants-with-food-protein-induced-enterocolitis-syndrome-a-single-tertiary-centre-australian-cohort-study

Hosted file

`Figure 4.pdf` available at https://authorea.com/users/362811/articles/483826-demographic-profile-food-trigger-associations-and-trends-in-outcome-of-infants-with-food-protein-induced-enterocolitis-syndrome-a-single-tertiary-centre-australian-cohort-study