TITLE: Allergic gastroenteritis hospital admission time trends in Australia and New Zealand 1998-2016

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KEYWORDS

Allergic gastroenteritis; anaphylaxis; epidemiology; food allergy.

ABBREVIATIONS

AG	Allergic gastroenteritis
FA	Food allergy
FPIES	Food protein induced enterocolitis syndrome

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The authors report no conflicts of interest.

ABSTRACT

Aim

Recent epidemiological studies indicate increases in hospital food allergy-related anaphylaxis admission rates in Australian and New Zealand. The aim of the study was to examine whether non-IgE mediated food allergy might have increased in parallel.

Methods

We analysed childhood hospital admissions rates by ICD 10 codes for allergic gastroenteritis (AG) and infective gastroenteritis in Australia and New Zealand between June 1998 and July 2014.

Results

In Australia most AG-related admissions (73%) occurred in those aged <1 year and increased by 7.3%/year (95%CI 5.5-9.3, P<0.0001) from 6.8 to 26.5/10^5 population. Similar trends were observed for New Zealand; 81% of admissions occurred in those aged <1 year and increased by 9.4%/year (95%CI 5.5-9.3, P<0.0001) from 7.2 to 30.7/10^5 population. By contrast there were no significant changes in AG-related admission rates in the older patients and infective gastroenteritis admissions fell in both countries in those aged < 1 year; Australia by 4.4%/year (95%CI 4.3-4.6, P<0.0001) and in New Zealand by 5.8%/year (95%CI 5.4-6.2, P<0.0001).

Conclusions

We observed a four-fold increase in AG-related admission rates in two countries with known high rates of IgE-mediated food allergy/anaphylaxis. If confirmed by other studies, it will be of interest to determine if factors thought to contribute to the increase in IgE-mediated FA[8] might also play a role in non-IgE mediated gastroenterological FA syndromes.

What is known on this topic

- IgE-mediated childhood food allergy has increased over the last 20 years in Australia and New Zealand.
- It is unknown whether non-IgE-mediated food allergy has increased as well.

What this paper adds

- Hospital admissions for allergic gastroenteritis (but not infective gastroenteritis) increased four-fold between 1998 and 2014.
- If this represents a true increase (and not greater recognition), it remains uncertain whether the same risk factors for IgE-mediated food allergy are relevant for non-IgE-mediated food allergy.

Introduction

Epidemiogical data (e.g. hospitalization rates) indicate that IgE-mediated food allergy (FA) and anaphylaxis has increased over the past 2 decades[1, 2]. With the possible exception of eosinophilic esophagitis[3] and coeliac disease, it is unclear whether other non-IgE mediated FA may have increased as well. "Allergic gastroenteritis" (AG) as classified under the International Statistical Classification of Diseases (ICD-10) encompasses a number of non-IgE mediated allergic conditions, including food protein-induced enterocolitis syndrome (FPIES), eosinophilic enteritis and colitis, food protein-induced enteropathy, "other allergic dietetic gastroenteritis and colitis", food hypersensitivity enteritis and colitis (but specifically not eosinophilic oesophagitis or coeliac disease). We sought to determine whether AG-related paediatric hospital admission rates have increased in parallel with increases in food-related IgE-mediated anaphylaxis in Australia and New Zealand

Methodology

We obtained ICD-10 classified hospital admissions data, as collected by the Australian Institute of Health and Welfare and the New Zealand Ministry of Health. Hospital admissions between July 1998 (Australia) or July 2000 (New Zealand) to June 2014 attributed to AG (K52.2) were examined. Infective gastroenteritis admissions (A0 to A9) and all cause admissions (available for Australia only) were examined as comparators to control for any trend for overall increased hospitalisation for gastrointestinal disorders that may have confounded analysis. Age ranges of < 1 year, 1-4 years and 5-14 years were selected to facilitate comparison with other admissions-related studies[2]. More

detailed codes for FPIES (K52.21), food protein-induced enteropathy (K52.22) or the term "other allergic dietetic gastroenteritis and colitis" (K52.29) were unavailable from the institutions providing data (AIHW, NZ MoH). Data are expressed as rates/10^5 population using concurrent national population data[2]. Time trends were analyzed using Poisson regression with year as a continuous predictor and total population as exposure variable. Analysis was performed using SAS 9.3 statistical software. The Human Research and Ethics committee of Calvary Bruce/Calvary John James Private Hospitals, Canberra, Australia approved the study.

Results

Hospital admissions for AG increased over the study period in Australia and New Zealand. In Australia most AG-related admissions (73%) occurred in those aged <1 year with slight male predominance (58%) and increased by 7.3%/year (95%CI 5.5-9.3, P<0.0001) from 6.8 to 26.5/10^5 population (**Table 1, Figure 1A**).

Similar trends were observed in New Zealand AG-related admissions; 81% occurred in those aged <1 year with slight male predominance (59%) and increased by 9.4%/year (95%CI 5.5-9.3, P<0.0001) from 7.2 to 30.7/10^5 population (**Figure 1B**). By contrast there were no significant changes in AG-related admission rates in the two older age groups in either country (**Table 1**).

When infective gastroenteritis admissions were examined as comparators, these decreased in Australia by 4.4%/year (95%CI 4.3-4.6, P<0.0001) and in New Zealand by 5.8%/year (95%CI 5.4-6.2, P<0.0001) in those aged <1 year. In

Australia there was a minor decrease in all-cause admissions of 0.1%/year (95%CI 0-0.1, P=0.0001).

Discussion

We report a 4-fold increase in AG-related hospital admission rates for AG in Australia and New Zealand in infants aged <1 year between 1998/99 and 2013/14. These trends (with slight male predominance and very similar rates between the two countries) could not be explained by increases in overall hospitalization rates, or consistent changes in admission rates for potentially mimicking conditions such as infective gastroenteritis ~~admissions~~admissions, which decreased over the period of observation (likely related to update of rotavirus immunization). AG-related admissions were almost absent in older Australasian age groups.

Many epidemiological studies rely upon ICD coding to track changes in rates of disease, or changes of distribution and burden of diseases within populations. In addition to the many potential caveats involved in using coding data of this nature[3] there are as yet unresolved questions about exactly what the K52.2 ICD code represents in practice and how coders are interpreting admissions data to make this decision about the admission. Accurate coding also relies upon the diagnostic expertise of the health professionals making the diagnosis during the hospital admission. The code is designed to identify food protein-induced enterocolitis syndrome (FPIES), eosinophilic enteritis and colitis, food protein-induced enteropathy, food hypersensitivity enteritis and colitis but specifically not eosinophilic oesophagitis or coeliac disease. While it would have been

informative to examine more detailed disease specific codes, such data is not available for Australia or New Zealand at this time.

Overall, our data suggest a possible increase in non-IgE-mediated FA related disorders such as has been already reported with eosinophilic esophagitis diagnostic rates[3] and is consistent with reports of increasing FPIES presentations to large allergy referral centres in Australia[4] and Italy[5] although not the USA[6]. While it is interesting to speculate that the increases in infant AG admissions might represent FPIES, with increases in infants presenting with the profuse vomiting, pallor and hypotension characteristic of FPIES requiring admission (rather than emergency department assessment and discharge), such conclusions are precluded by the limitations of coding data and thus inability to differentiate from other related conditions (eg. food induced enteropathy with failure to thrive) or mimicking conditions (infective gastroenteritis). The observation that rates of admission for AG in both countries for the <1 year age group were very similar is supportive of the possibility that the majority of these cases represent FPIES. If the increase in AG is confirmed by other studies, and not an solely an artefact of improved recognition of disorders such as FPIES[7] and coding, it will be of interest to determine if factors thought to contribute to the increase in IgE-mediated FA[8] might also play a role in non-IgE mediated gastroenterological FA syndromes.

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TABLE 1 LEGEND

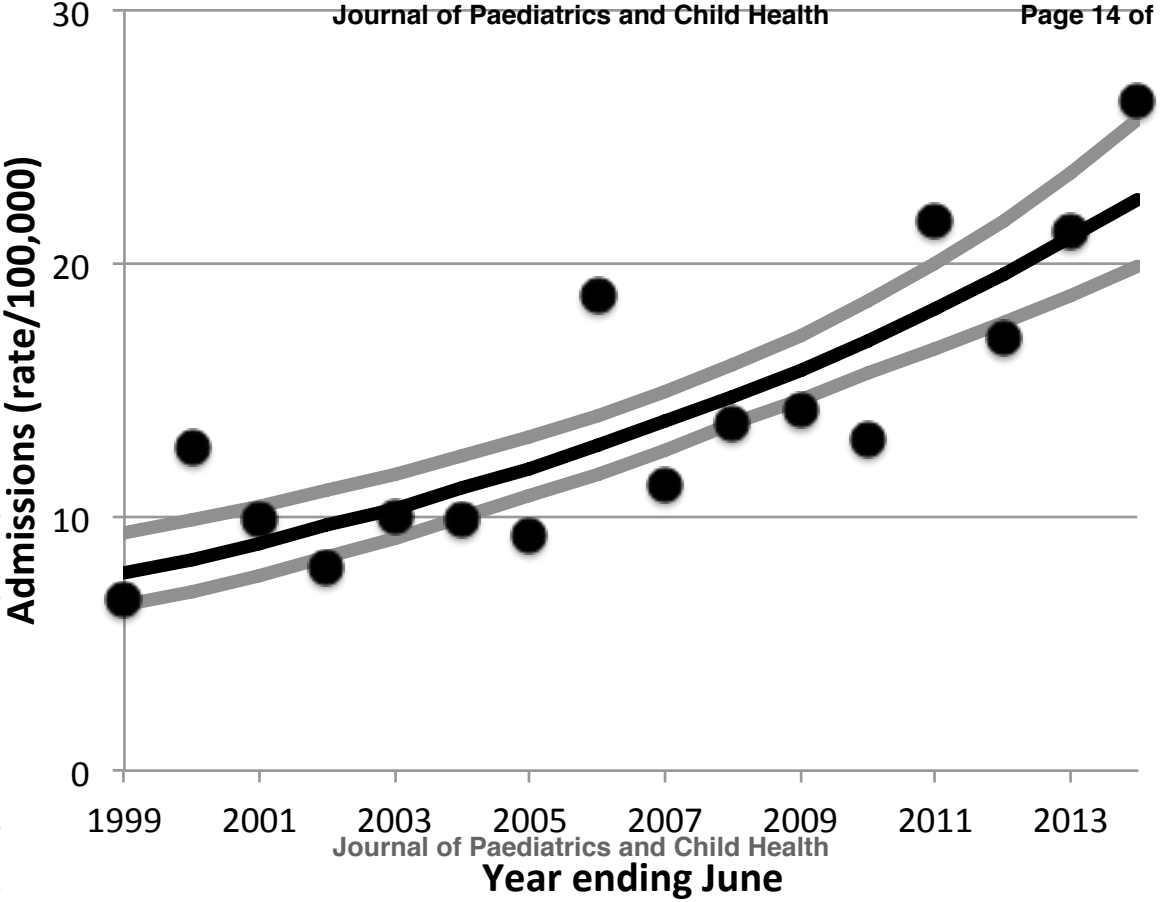
Time trends in hospital admissions rates for allergic gastroenteritis and infective gastroenteritis

FIGURE LEGENDS

Figure 1

Allergic gastroenteritis admissions in children aged less than 1 year

Admission rates are shown for (a) Australia and (b) New Zealand with trends lines (black lines) and 95% CI (grey lines).


30
20
10
0
Admissions (rate/100,000)
1999
2001
2003
2005
2007
2009
2011
2013
Journal of Paediatrics and Child Health
Year ending June

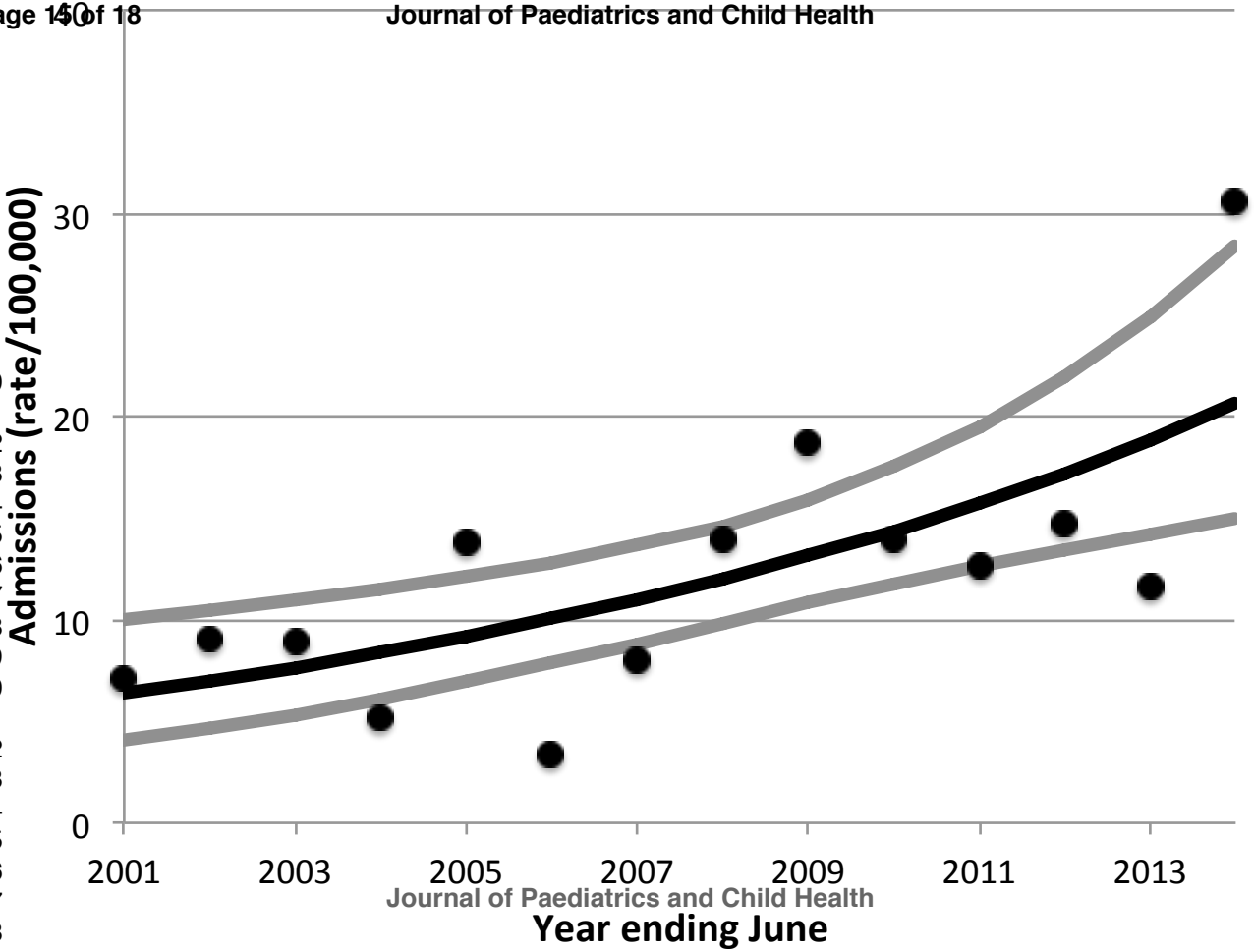

40
30
20
10
0
Admissions (rate/100,000)
2001
2003
2005
2007
2009
2011
2013
Year ending June
Journal of Paediatrics and Child Health

TABLE 1

Condition	No.	Rate/100,000 1998(Aust); 2000(NZ)	Rate/100,000 2014	% change/year	Lower CI	Upper CI	P value
		AUSTRALIA					
Allergic gastroenteritis							
< 1 year	633	6.8	26.5	7.3	5.5	9.3	<0.0001
1-4 years	167	0.5	1.5	2.6	-0.8	6	0.13
5-14 years	62	0.2	0.1	5	-0.6	10.9	0.081
Infectious gastroenteritis							
< 1 year	73,132	2179.0	1243.3	-4.4	-4.3	-4.6	<0.0001
1-4 years	169,926	1222.0	486.2	-7.1	-7	-7.2	<0.0001
5-14 years	80518	171.2	158.7	-1.1	-1	-1.3	<0.0001
Total admissions							
< 1 year	2,388,538	54933.2	57820.2	-0.1	0	-0.1	<0.0001
1-4 years	2,848,250	17783.5	15787.5	-0.9	-0.9	-1	<0.0001
5-14 years	3,784,606	8622.6	9047.6	0.5	0.5	0.5	<0.0001
		NEW ZEALAND					
Allergic gastroenteritis							
< 1 year	104	7.2	30.7	9.4	4	15.1	0.0005
1-4 years	22	0.4	0.4	1.4	-8.6	12.5	0.79
5-14 years	2	0	0	-9	-30	36.4	0.61
Infectious gastroenteritis							
< 1 year	12278	1885.6	864.7	-5.8	-5.4	-6.2	<0.0001
1-4 years	20320	829.6	368.5	-6.7	-6.4	-7	<0.0001
5-14 years	7058	95.5	55.6	-6.4	-5.8	-6.9	<0.0001

Table 1

Condition	Gender	No.	Rate/100,000 Aust(1998); NZ(2000)	Rate/100,000 2014	% change/year	Lower CI	Upper CI	P value
			AUSTRALIA					
Allergic gastroenteritis								
< 1 year	Male	364	7.8	27.4	5.3	2.9	7.8	<0.0001
	Female	269	5.7	25.5	10.3	7.2	13.4	<0.0001
	Total	633	6.8	26.5	7.3	5.5	9.3	<0.0001
1-4 years	Male	106	0.8	1.4	-0.4	-3.8	4.4	0.86
	Female	64	0.2	1.5	7.9	2	4.1	0.0082
	Total	167	0.5	1.5	2.6	-0.8	6	0.13
5-14 years	Male	32	0.1	0.2	8.3	0.1	17.1	0.0465
	Female	30	0.2	0.1	1.7	-5.8	10	0.66
	Total	62	0.2	0.1	5	-0.6	10.9	0.081
Infectious gastroenteritis								
< 1 year	Male	39,380	2293.5	1267.1	-0.46	4.4	4.8	<0.0001
	Female	33,752	2058.8	1218.3	-4.2	-4	-4.4	<0.0001
	Total	73,132	2179.0	1243.3	-4.4	-4.3	-4.6	<0.0001
1-4 years	Male	88,708	1253.2	498.3	-7	-6.9	-7.1	<0.0001
	Female	81,218	1189.1	473.4	-7.1	-7	-7.3	<0.0001
	Total	169,926	1222.0	486.2	-7.1	-7	-7.2	<0.0001
5-14 years	Male	42181	177.2	161.8	-1.1	-0.8	-1.3	<0.0001
	Female	38337	164.9	155.3	-1.2	-1	-1.4	<0.0001
	Total	80518	171.2	158.7	-1.1	-1	-1.3	<0.0001
			NEW ZEALAND					
Allergic gastroenteritis								
< 1 year	Male	61	14	39.8	11.2	4	19	0.0019
	Female	43	0	21.1	7	-1	15.6	0.0865
	Total	104	7.2	30.7	9.4	4	15.1	0.0005
1-4 years	Male	15	0.9	0.8	9.7	-3.9	25.2	0.17
	Female	7	0	0	-14.4	-4.7	30.1	0.13
	Total	22	0.4	0.4	1.4	-8.6	12.5	0.79

5-14 years	Male	1	0	0	-22.7	-47	59.4	0.43
	Female	1	0	0	3.2	-37	68.2	0.9
	Total	2	0	0	-9	-30	36.4	0.61
Infectious gastroenteritis								
< 1 year	Male	6683	1996.5	881.7	-5.7	-5.2	-6.3	<0.0001
	Female	5595	1770.1	8482.8	-5.9	-5.2	-6.5	<0.0001
	Total	12278	1885.6	864.7	-5.8	-5.4	-6.2	<0.0001
1-4 years	Male	10746	883.6	385.6	-6.8	-6.4	-7.3	<0.0001
	Female	9574	772.7	350.5	-6.5	-6	-7	<0.0001
	Total	20320	829.6	368.5	-6.7	-6.4	-7	<0.0001
5-14 years	Male	3725	93.2	59.3	-5.8	-5	-6.6	<0.0001
	Female	3333	97.9	51.8	-7	-6.2	-7.8	<0.0001
	Total	7058	95.5	55.6	-6.4	-5.8	-6.9	<0.0001