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Guidance on cow's milk allergy may be fuelling overdiagnosis in infants, study finds

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International guidelines designed to help doctors diagnose cow's milk allergy in infants may be leading to overdiagnosis of the condition, researchers have warned.¹

The team from the University of Bristol, St George's University of London, and King's College, London assessed 1300 infants and found that nearly three quarters (74%) of those aged 3-12 months exhibited mild to moderate symptoms outlined in the international Milk Allergy in Primary Care (iMAP) guideline.²

Rosie Vincent, study lead and an honorary clinical research fellow at the University of Bristol, said, "Guidelines designed to help the non-specialist to diagnose cow's milk allergy in infants may unintentionally medicalise normal infant symptoms and promote overdiagnosis of cow's milk allergy."

The findings come after an investigation by *The BMJ* found that prescriptions of specialist formula milk for infants with cow's milk protein allergy in England and Wales increased by nearly 500% from 2006 to 2016.³ Over the same period NHS spending on these products in England increased by nearly 700%.

This was despite epidemiological data giving no indication that such a large increase in true prevalence had occurred. The report indicated that cow's milk protein allergy was possibly being used by the global formula industry to build relationships with healthcare professionals and drive overdiagnosis.

Symptoms

The latest research, published in *Clinical and Experimental Allergy*,¹ used data from the Enquiring About Tolerance study, in which parents were asked to record monthly any symptoms their child experienced. The research team counted how many infants had symptoms of cow's milk allergy each month, which include possetting, vomiting, colic, loose stools or constipation, and flaring of eczema.

The researchers focused on non-immunoglobulin E-mediated cow's milk allergy, which is thought to affect around 1% of people in European countries. Unlike IgE-mediated cow's milk allergy, which causes immediate and consistent symptoms and can be diagnosed through testing, this type typically has delayed symptoms, and diagnosis relies on observing clinical improvement when cow's milk protein is avoided.

Cow's milk protein is commonly consumed by infants through standard infant formula or in foods containing milk, and very small quantities of the protein lactoglobulin (a major allergen in cow's milk) can also be found in breast milk.

Rising prescription rates

The study found that one in four parents reported two or more possible "mild to moderate" symptoms in their child every month. The proportion of children affected was highest at age 3 months, when none of the children were fed cow's milk, in both two or more mild to moderate symptoms (37.6%) and two or more severe symptoms (4.3%).

At age 3-6 months half of the infants were given six allergenic foods, including cow's milk, introduced alongside breastfeeding. The other half were exclusively breastfed until around 6 months.

The researchers found that at 6 months of age there was no significant difference between the two groups in the number of children with two or more symptoms.

Michael Perkin, senior co-researcher and honorary consultant in paediatric allergy at St George's University of London, said, "Our findings come against a background of rising prescription rates for specialist formula for children with cow's milk allergy, which is completely out of proportion to how common we know the condition is."

"Parents of young infants are often seen in clinics, worried about a medical cause for their infant's symptoms such as colic, bringing up milk, or loose stools. However, our research confirms that these symptoms are extremely common. In an otherwise healthy infant, an underlying cause is unlikely. Incorrectly attributing these symptoms to cow's milk allergy is not only unhelpful but may also cause harm by discouraging breastfeeding."

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- 2 Venter C, Brown T, Meyer R, 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. doi: 10.1186/s13601-017-0162-y. pmid: 28852472
- 3 Van Tulleken C. Overdiagnosis and industry influence: how cow's milk protein allergy is extending the reach of infant formula manufacturers. *BMJ* 2018;363:k5056doi: 10.1136/bmj.k5056.