

- Hosakoppal SS, Bryce PJ. Transplant-acquired food allergy: current perspectives. *J Asthma Allergy*. 2017;10:307–315.
- Needham JM, Nicholas SK, Davis CM. Food allergies developing after solid organ transplant. *Pediatr Transplant*. 2015;19(8):827–835.
- Hernandez-Ojeda A, Rojas N, Barriga F, Wietstruck MA, Morales PS, Borzutzky A. Incidence and risk factors of food allergy after umbilical cord blood transplantation in children. *J Allergy Clin Immunol Pract*. 2017;5(6):1789–1791.
- De Bruyne R, Dullaers M, Van Biervliet S, et al. Post-transplant food allergy in children is associated with liver and not with renal transplantation: a monocentric comparative study. *Eur J Pediatr*. 2013;172(8):1069–1075.
- Marcus N, Amir AZ, Grunebaum E, et al. De novo allergy and immune-mediated disorders following solid-organ transplantation—prevalence, natural history, and risk factors. *J Pediatr*. 2018;196:154–160.e152.
- Ozbek OY, Ozcaý F, Avci Z, Haberal A, Haberal M. Food allergy after liver transplantation in children: a prospective study. *Pediatr Allergy Immunol*. 2009;20(8):741–747.
- Snyder AB, Lane PA, Zhou M, Paulukonis ST, Hulihan MM. The accuracy of hospital ICD-9-CM codes for determining Sickle Cell Disease genotype. *J Rare Dis Res Treat*. 2017;2(4):39–45.

The clinical presentation of alpha-gal allergy among pediatric patients with food allergy in southwest Missouri



Alpha-gal allergy is associated with immunoglobulin E (IgE) antibodies to galactose- α -1,3-galactose (alpha-gal), a carbohydrate found in beef, pork, and lamb. First described in the adult population in 2009 by Commins et al,¹ this syndrome is associated with delayed anaphylaxis, angioedema, and urticaria with symptom onset 3 to 6 hours after eating red meat.^{1–3} Bites from ticks, namely the Lone Star Tick (*Amblyomma americanum*) in the United States, are associated with production of IgE antibodies to alpha-gal, resulting in an immune system primed to react to foods containing the antigen in patients who previously tolerated meat without symptoms.^{3,4}

The epidemiology and clinical features of alpha-gal syndrome in pediatric patients are not well studied. Lack of awareness for this allergy may lead to a delay in diagnosis and failure to avoid the offending agent, thus increasing the patient's risk of a severe systemic reaction.^{4–6} This study aimed to determine the clinical presentation of alpha-gal syndrome among pediatric patients with documented food allergy in southwest Missouri. A greater understanding of the prevalence and clinical presentation will help physicians determine when to test patients for IgE to alpha-gal as a potential cause of their symptoms.^{4–6}

Using Healthe Analytics by Cerner, we recruited patients retrospectively for the study from one of southwest Missouri's largest health care systems with a catchment area spanning from northern Arkansas toward the central region of Missouri. The study determined the total number of pediatric food allergy patients ages 0 to 18 years based on food allergy ICD10 codes. Similarly, we used Healthe Analytics to generate an initial list of pediatric patients with alpha-gal sensitization based on an IgE level greater than 0.35 kU/L from 2014 to 2018. From this list, we accessed each patient's chart to confirm the presence of a true alpha-gal allergy based on clinical presentation consistent with a delayed allergic reaction 3 to 6 hours after red meat consumption in addition to elevated IgE levels against alpha-gal.^{1,2}

We used this information to determine the prevalence of alpha-gal syndrome among pediatric patients with documented food allergies. With the earliest diagnosis recorded in November 2014 in our system, our prevalence calculation includes all reported alpha-gal diagnoses from 2014 to 2018 among patients currently 18 years of age or younger from multiple clinics in southwest Missouri. We determined incidence based on new diagnoses from January 1, 2018 to December 31, 2018. Alpha-gal patient charts were accessed individually to identify sex, age of diagnosis, clinical presentation, history of emergency room management, and prior physician diagnosis of allergic rhinitis, eczema, and asthma (Table 1).

A total of 1268 patients with documented food allergy between the ages of 0 and 18 years in southwest Missouri were included in the study. Of these patients, 42 were diagnosed with alpha-gal syndrome based on elevated IgE levels against alpha-gal as well as a history of a delayed allergic reaction after red meat consumption. The prevalence of alpha-gal syndrome in southwest Missouri among pediatric food allergy patients was 3.31%, with an incidence of 0.87% during 2018. The mean age of diagnosis was 9.95 years with a range from 3 years to 17 years of age. Slightly more patients were male at 57.14% (24 of 42).

Urticaria was the most common presentation, accounting for 78.05% (32 of 41) of cases. From most to least prevalent, other presentations included anaphylaxis, angioedema, and gastrointestinal symptoms. Many of these reactions were severe with 32.5% (13 of 40) of patients requiring emergency room management for their symptoms. Levels of IgE antibody ranged from 0.38 to 67.7 kU/L with a geometric average of 2.94 kU/L. Most alpha-gal patients at 78.05% (32 of 41) reported a history of eczema, allergic rhinitis, or asthma with allergic rhinitis reported in 68.39% (28 of 41) of cases. Approximately 19.5% (8 of 41) of alpha-gal patients reported asthma and 9.76% (4 out of 41) reported eczema.

No prior studies have reported the prevalence of alpha-gal syndrome in the pediatric population to our knowledge. Our study found a prevalence of 3.31% among pediatric patients with a documented food allergy in southwest Missouri. The range of clinical presentation of our alpha-gal patient population showed similar results to prior studies with urticaria as the most common symptom.³ Compared Wilson et al,³ fewer patients in our study presented with gastrointestinal symptoms. This may be attributable to a lower level of suspicion among clinicians for alpha-gal syndrome as well as greater consideration of alternative diagnoses in pediatric patients presenting with gastrointestinal symptoms compared with those presenting with more typical presentations of food allergy, such as urticaria or anaphylaxis. While almost half of patients required emergency room management in Kennedy et al,⁴ only one-third of patients in our study presented to the emergency room. Although our study focuses on pediatric cases, our results show similar prevalence of allergic conditions compared with Wilson et al,³ with 68.3% of patients diagnosed with allergic rhinitis and 19.5% diagnosed with asthma.

Although we accessed each alpha-gal patient's chart to determine the presence of true alpha-gal allergy, a drawback of our study was using Healthe Analytics to generate an initial list of pediatric food allergy patients based on ICD10 codes and age. We did not access these patients' charts individually to determine the presence of a true food allergy based on allergic symptoms in response to consumption of a specific food. This may dilute our calculated prevalence of alpha-gal among pediatric patients. Future

Table 1
Clinical Features of Alpha-Gal

Prevalence (2014–2018)	3.31%
Incidence (2018)	0.87%
Sex (% male) (n = 42)	57.14%
Average age of diagnosis (n = 42)	9.95 years
Clinical presentation (n = 41)	
Urticaria (%)	32 (78.04%)
Anaphylaxis (%)	12 (29.27%)
Angioedema/facial swelling (%)	9 (21.95%)
Gastrointestinal-related (%)	7 (17.07%)
ED management (%) (n = 40)	13 (32.50%)

Abbreviation: ED, emergency department.

studies may focus on comparison of alpha-gal IgE with total IgE levels, long-term follow-up of symptoms and alpha-gal IgE levels, IgE levels against specific meat allergens, and age of symptom onset.

To our knowledge, this study represents the first epidemiology study of the alpha-gal allergy in the pediatric population in Missouri. Our study shows the prevalence and clinical presentation of the alpha-gal syndrome among pediatric patients diagnosed with food allergy. Our results highlight the importance of considering alpha-gal syndrome among patients presenting with delayed allergic reactions to mammalian meat.

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References

1. Commins SP, Satinover SM, Hosen J, et al. Delayed anaphylaxis, angioedema, or urticaria after consumption of red meat in patients with IgE antibodies specific for galactose- α -1, 3-galactose. *J Allergy Clin Immunol*. 2009;123:426–433.
2. Khoury JK, Khoury NC, Schaefer D, Chitnis A, Hassen GW. A tick-acquired red meat allergy. *Am J Emerg Med*. 2018;36: 341–341.
3. Wilson JM, Schuyler AJ, Workman L, et al. Investigation into the α -gal syndrome: characteristics of 261 children and adults reporting red meat allergy. *J Allergy Clin Immunol Pract*. 2019. <https://doi.org/10.1016/j.jaip.2019.03.031>.
4. Kennedy JL, Stallings AP, Platts-Mills TA, et al. Galactose- α -1, 3-galactose and delayed anaphylaxis, angioedema, and urticaria in children. *Pediatrics*. 2013;131: 1545–1552.
5. Carter MC, Ruiz-Estevés KN, Workman L, Lieberman P, Platts-Mills TAE, Metcalfe DD. Identification of alpha-gal sensitivity in patients with a diagnosis of idiopathic anaphylaxis. *Allergy*. 2017;73:1131–1134.
6. Pattanaik D, Lieberman P, Lieberman J, Pongdee T, Keene AT. The changing face of anaphylaxis in adults and adolescents. *Ann Allergy Asthma Immunol*. 2018; 121:594–597.