

## LETTER TO EDITOR (VIEWERS CHOICE)

## SERUM TRYPTASE CONCENTRATION - THE IMPORTANCE OF INDIVIDUALIZED CLINICAL AND ANALYTICAL EVALUATION

Rita Calejo<sup>1,2</sup>, Joana Carvalho Queirós<sup>3,2</sup>, João Nogueira Oliveira<sup>3,2</sup>, Diana Pinto<sup>2</sup>, Fernanda Teixeira<sup>2</sup>, Ana Rita Araújo<sup>2</sup>.

<sup>1</sup>Pediatrics and Neonatology Department, Tâmega e Sousa Local Health Unit, Portugal,

<sup>2</sup>Pediatric Allergology Unit, Pediatrics Department, Santo António Local Health Unit, Portugal,

<sup>3</sup>Pediatrics Department, Santo António Local Health Unit, Portugal.Fonseca, EPE, Amadora, Portugal.

### KEYWORDS

Tryptase, Anaphylaxis, Hereditary alpha-tryptasemia, Mastocytic Activation.

### ARTICLE HISTORY

Received 04 Oct 2024

Accepted 24 Dec 2024

Tryptase is the most common proteolytic enzyme that comes from mast cell secretory granules. This quantitative test, which is carried out in serum or plasma, typically indicates mast cell activation, which is most commonly linked to allergic reactions.<sup>1,2,3</sup> Tryptase increase can occur in anaphylactic reactions, but it is not pathognomonic of the diagnosis, and its absence does not rule it out. Serum tryptase levels typically range from 0 to 11.4 ug/L (0-11,4 ng/mL).<sup>1</sup> To increase awareness of the different possibilities of the tryptase evolution, the authors present three clinical situations in which the serum tryptase levels can be interpreted differently.

The most common and well recognized situation is similar to this 10-month-old infant girl, previously healthy, that was evaluated at the emergency room due to the development of a widespread rash and copious vomiting 20 minutes after ingesting cashew nuts. The blood tests showed an elevation of the tryptase level (26 ng/mL). At the follow up appointment blood test results revealed a positive recombinant cashew 2S albumin, rAna o 3 of 5,8 ISU-E, and the basal tryptase of 4 ng/mL.

However, tryptase can have a different presentation, such as in this 3-month-old boy who was previously diagnosed with atopic dermatitis and brought to the emergency room due to vomiting and a widespread rash that emerged right after receiving the meningococcal ACWY vaccination. Following the event, the tryptase level was 14.4 ng/mL. Reevaluation of the basal tryptase was 21.7 ng/mL, 1.5 months later. Serum tryptase levels remained elevated even after subsequent repeated dosages. A family investigation of the tryptase levels was conducted considering the hypothesis of hereditary alpha-tryptasemia. The mother's baseline level was 13,8 ng/mL and the father's was 5,68 ng/mL. The elevation of both the infant and his mother tryptase values led to genetic testing that confirmed Hereditary alpha-tryptasemia with an extra copy of the TPSAB1 gene.

The less recognized situation can be illustrated by a 18-month-old boy, without previous history of allergic reactions and complementary feeding that underwent without any complications until 12 months, that presented later numerous episodes of anaphylactic reaction with a myriad of foods (egg white, cow's milk protein, soy, wheat, apple, peach). During these events, the determined tryptase levels varied from 7,7 to 11,4 ng/mL. Serum tryptase levels were 4,2 ng/mL at baseline. Considering the equation – tryptase value during a crisis  $>(1.2 \times \text{basal tryptase value}) + 2$  - that proves mastocyte activation<sup>1,6,7</sup>, confirming severe allergic reactions: values during the crisis  $>7,04 = [(1.2 \times 4,2) + 2]$ .

The first situation is the most typical and well recognized by all clinicians, which is the characteristic rise of the tryptase value followed by normalization associated with a severe allergic reaction.<sup>1,2,3</sup> Before a consistent elevation of baseline tryptase concentration, the second case should raise awareness for the diagnosis of hereditary alpha-tryptasemia, preventing misinterpretations of severe allergic reactions.<sup>1,2,3,4,5</sup> About 5% of people worldwide are afflicted with this disease, a recently identified autosomal dominant condition marked by an excess of TPSAB1 gene copies.<sup>1,2,3,4,5</sup> The third case shows absence of a tryptase level superior to the normal range even in episodes compatible with anaphylaxis. Serum tryptase concentrations are elevated in cases of anaphylaxis due to degranulation of mast cells, but this mastocyte activation does not always surpasses the upper limit level, due to the natural variation across the population.<sup>6,7</sup> An equation was developed during the 2010 Working Conference on Disorders of Mast Cells to specify the lowest level of serum tryptase increase over an individual's baseline that meets the requirements to characterize a significant systemic mastocyte activation present in an anaphylactic reaction: The most appropriate value for peak mast cell tryptase is  $>1.2$  times baseline tryptase  $+ 2$  ng/mL.<sup>1,2,3,6,7</sup>

Tryptase can exhibit unique behaviors depending on the clinical circumstances, reflecting several interpretations that medical professionals ought to be aware of. Assessing this biomarker's progression rather than a single isolated result is crucial, as is incorporating

**Address for Correspondance:** Rita Calejo, Pediatrics and Neonatology Department, Tâmega e Sousa Local Health Unit, Portugal.

**Email:** ritacalejor@gmail.com

©2025 Pediatric Oncall

it into the clinical and additional analytical context. Hereditary alpha-tryptasemia and mastocyte activation with normal tryptase levels are two examples of less frequent but nonetheless significant variants of this biomarker.

**Compliance with Ethical Standards****Funding** None**Conflict of Interest** None**References:**

1. H. Lobbes, Q. Reynaud, S. Mainbourg, J.C. Lega, I. Durieu, S. Durupt. Dosage de la tryptase : un guide d'utilisation pour le clinicien, *La Revue de Médecine Interne*, Volume 41, Issue 11, 2020. Pages 748-755. ISSN 0248-8663.
2. Pongdee T, Castells M. Elevated Tryptase: Conditions and Pitfalls. *J Allergy Clin Immunol Pract*. 2022 Sep;10(9):2436-2437. doi: 10.1016/j.jaip.2022.06.028. PMID: 36087946.
3. Michel M, Klingebiel C, Vitte J. Tryptase in type I hypersensitivity. *Ann Allergy Asthma Immunol*. 2023 Feb;130(2):169-177. doi: 10.1016/j.anai.2022.08.996. Epub 2022 Sep 7. PMID: 36084866.
4. Le Blanc V, Watson WTA. Elevated tryptase level in a child with idiopathic anaphylaxis: a case of hereditary alpha-tryptasemia. *Allergy Asthma Clin Immunol*. 2024 Mar 27;20(1):26. doi: 10.1186/s13223-023-00858-4. PMID: 38539267; PMCID: PMC10976751.
5. Lee AYS. Elevated Serum Tryptase in Non-Anaphylaxis Cases: A Concise Review. *Int Arch Allergy Immunol*. 2020;181(5):357-364. doi: 10.1159/000506199. Epub 2020 Mar 3. PMID: 32126554.
6. Valent P, Bonadonna P, Hartmann K, Broesby-Olsen S, Brockow K, Butterfield JH et al. Why the 20% + 2 Tryptase Formula Is a Diagnostic Gold Standard for Severe Systemic Mast Cell Activation and Mast Cell Activation Syndrome. *Int Arch Allergy Immunol*. 2019;180(1):44-51. Epub 2019 Jun 28. PMID: 31256161; PMCID: PMC7115850.
7. Passia E, Jandus P. Using Baseline and Peak Serum Tryptase Levels to Diagnose Anaphylaxis: a Review. *Clin Rev Allergy Immunol*. 2020 Jun;58(3):366-376. doi: 10.1007/s12016-020-08777-7. PMID: 32034676.