Dear Editor,

We read the case study of a 43-year-old man, who was a tobacco smoker and no alcoholic beverage consumer, who presented with episodes of mild epigastric pain and abdominal bloating, with triglycerides: 90–1,086 mg/dL, amylase: 212–669 U/L, and normal serum lipase.1) Serum and urinary amylase and creatinine levels were used to determine the amylase creatinine clearance ratio (ACCR), which was 0.155%, indicative of macroamylasemia.1) Notably, macroamylasemia was not an initially suspected in this case, and evidence of hypertriglyceridemia raised the suspicion of acute pancreatitis. The authors emphasized the role of ACCR in patients with elevated serum amylase levels concomitant with both normal serum lipase levels and normal urinary amylase levels. Cost-effective confirmation of macroamylasemia avoids invasive tests or treatments.1) As macroamylasemia is estimated to affect approximately 1% of the general population and 2.5% of people with hyperamylasemia, the possibility of misdiagnosis with pancreatitis is high; therefore, the objective of the following comments is to enhance the suspicion index.2-5) Čázenská et al.2) studied 13 asymptomatic individuals with a mean age of 40.8 years with isolated macroamylasemia without pancreatic disease and normal renal function. Macroamylase was confirmed in five of them by the polyethylene glycol precipitation (PEG) method, and the polyethylene glycol precipitation activity (%PPA) in suspected patients was 89.1% for amylase and 84.3% for pancreatic amylase.2) The %PPAs in the control samples were 29.6% for amylase and 32.2% for pancreatic amylase. The %PPA for immunoglobulin G, immunoglobulin A 58.0%, and immunoglobulin M were similar in the suspected samples and controls.2) The authors highlighted the macrocomplexes as benign processes in healthy individuals.2) Choi3) reviewed the mechanisms underlying elevated serum amylase and lipase levels, associated conditions, and diagnostic resources for managing these patients. In macroamylasemia, a combination of amylase with large molecules acts as an example of immunoglobulins and polysaccharides, propitiating lower renal excretion and accumulation in the bloodstream, increasing serum amylase levels.3) The author cited a study that included 2,900 patients with hyperamylasemia, and approximately 9.6% of them presented with macroamylasemia, which is more frequently asymptomatic, although it may be found in individuals with abdominal pain, nausea, vomiting, or diarrhea.3) Other associated causes include systemic lupus erythematosus, rheumatoid arthritis, Sjögren’s disease, Crohn’s disease, celiac disease, ulcerative colitis, immunoglobulin A deficiency, monoclonal gammopathy, myasthenia gravis, and human immunodeficiency virus infection.3) DeDeene et al.4) evaluated the upper reference limits (URLs) for amylase, creatine kinase, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, gamma-glutamyltransferase, lactate dehydrogenase, and lipase after PEG precipitation to detect macroenzymes and found adequate within-lab precision for all these enzymes. The authors emphasized that PEG precipitation is rapidly indicative of the presence of macroenzymes whenever the PEG-precipitable activity (%PPA) is above the URL.4) Lee et al.5) commented on the origin of amylase and lipase macroenzymes by linking them
to immunoglobulins and their accumulation in the blood due to lower glomerular filtration. They commented on the production and secretion of enzymes by the pancreas, salivary glands, malignant tumors (lung, esophagus, breast, and ovary), fallopian tubes, lungs, thyroid, tonsils, glands (mammary, lacrimal, and sweat), and adipose tissue.\(^5\)

They also emphasized an elevated suspicion index for a confirmed diagnosis of macroamylasemia in patients with a 24-hour urine ACCR less than 1\%.\(^5\)

In conclusion, both the first referenced study and the new data aim to increase the general interest of nonspecialists in this challenging matter.

**CONFLICT OF INTEREST**

No potential conflict of interest relevant to this article was reported.

**ORCID**

Vitorino Modesto dos Santos: https://orcid.org/0000-0002-7033-6074

Lister Arruda Modesto dos Santos: https://orcid.org/0000-0003-4647-4044

Taciana Arruda Modesto Sugai: https://orcid.org/0000-0002-4397-3254

**REFERENCES**