Echoes of the Past: The Intriguing Link between Chagas Disease and Insulin

Marcia M. Noya-Rabelo[1,2,3] *and Olga Souza*[1]

Instituto D'Or de Ensino e Pesquisa (IDOR),[1] *Salvador, BA – Brazil*
Escola Bahiana de Medicina e Saúde Pública – EBSMP,[2] *Salvador, BA – Brazil*
Hospital Aliança,[3] *Salvador, BA – Brazil*

Short Editorial related to the article: Decreased Insulin Levels in Patients with Acute Chagas Disease from Brazilian Amazon treated with Benznidazole

Chagas disease is currently classified as one of several neglected tropical diseases and as one of the five neglected parasitic infections prioritized by the World Health Organization and the Center for Disease Control for public health intervention.[1] This underscores the fact that the causative agent of American trypanosomiasis has existed for approximately 9.000 years, with positive samples dating back to 7050 B.C.[2] The life cycle of *Trypanosoma cruzi (T. cruzi)* comprises several morphological transformations involving both mammalian and vector hosts, where three different major developmental stages are identified: epimastigotes, trypomastigotes, and amastigotes.[3] Traditionally, *T. cruzi* is known to target the heart and gastrointestinal tract; however, its parasitism also results in structural changes and pro-inflammatory effects in adipose tissue and the pancreas.

In this edition of the *Arquivos Brasileiros de Cardiologia*, a longitudinal study by Barbosa-Ferreira et al.[4] evaluated the levels of insulin, adiponectin, and leptin before and after treatment of acute Chagas disease with benznidazole. Twenty-eight subjects were divided into two groups: a control group (15 subjects) and an acute Chagas disease group (13 subjects). The authors found no significant differences in serum levels of adiponectin and leptin between the groups. In contrast, serum levels of insulin were lower in the acute Chagas group, both before and after treatment, compared to the control group. Additionally, insulin levels were lower in the post-treatment phase compared to the pre-treatment phase.

Several studies have examined the consequences of *T. cruzi* infection on pancreatic function in rodents. Lenzi et al.[5] infected BALB/c mice with the CL strain of *T. cruzi* and sacrificed 15 days post-infection. There was diffuse interstitial pancreatitis associated with edema, infiltration of monocytes and macrophages, especially around intralobular ducts, and lobular atrophy, suggesting acinar cell loss. On the other hand, another group found amastigote nests in islets as well as pancreatic ducts and acini.[6] Presence of amastigotes in both the endocrine and exocrine pancreas was confirmed in infected mice in a separate study.[7]

The Santos et al.[8] group, employing a hamster model, investigated the consequence of *T. cruzi* infection on pancreatic β cells. Blood glucose and insulin levels in circulation were sampled in the animals during the acute phase as well as in the chronic phase. Plasma insulin concentrations were significantly lower in 6 out of 8 infected animals during both acute and chronic infection compared to uninfected control animals, so that overall, infected animals displayed lower insulin levels compared to controls. Hypoinsulinemia had already been described by other authors in murine models, and the causes may be multifactorial, such as a consequence of parasitism of the pancreas and of inflammation, fibrosis and atrophy of the subsequent parenchyma; insulinitis;[8] intrapancreatic ganglionitis;[9] abnormalities in pancreatic innervation, especially involving the parasympathetic nervous system;[8,10] and alteration of the enteroinsular axis related to autonomic dysfunction.[10]

The role of *T. cruzi* in regulating insulin secretion during infection of β cells has not been studied extensively in either humans or animal models. Review of the current human studies as to whether *T. cruzi* infection leads to hyperglycemia and diabetes, on the other hand, is inconclusive. In addition, decreased insulin secretion did not consistently correlate with increased prevalence of hyperglycemia.[11,12]

To date, our understanding of hormone secretion in patients with Chagas disease has primarily been derived from a limited number of clinical studies, many of which have small sample sizes. This article offers new insights into the complex pathophysiology of Chagas disease by adding information on insulin levels during the acute phase in humans.[4]

We also need to examine the extent to which the regulation and actions of *Trypanosoma cruzi* are either redundant or unique across different target organs. It is crucial to address whether selective control mechanisms in various tissues are involved, requiring coordination on a more global level. For instance, considering the role of insulin abundance and sensitivity as mediators of broad-range host-parasite interactions could pave the way for new strategies in parasitic control.

Keywords

Insulin; Acute Chagas Disease

Mailing Address: Marcia M. Noya-Rabelo •
Hospital Aliança – Diretoria Médica – Av. Juracy Magalhães Júnior, 2096. Postal Code 41920-180, Rio Vermelho, Salvador, BA – Brazil
E-mail: marcianoya@gmail.com
Manuscript received April 22, 2025, revised manuscript May 02, 2025, accepted May 02, 2025

DOI: https://doi.org/10.36660/abc.20250295i

References

1. Montresor A. Neglected Tropical Diseases. In: Raviglione MCB, Tediosi F, Villa S, Casamitjana N, Plasència A, editors. Global Health Essentials. Sustainable Development Goals Series. New York: Springer; 2023. p. 103-107. doi:10.1007/978-3-031-33851-9_16.
2. Aufderheide AC, Salo W, Madden M, Streitz J, Buikstra J, Guhl F, et al. A 9,000-Year Record of Chagas' Disease. Proc Natl Acad Sci USA. 2004;101(7):2034-9. doi: 10.1073/pnas.0307312101.
3. Solís-Oviedo RL, Monteon V, López R, Pech-Canul ÁC. Biochemical, Cellular, and Immunologic Aspects during Early Interaction between Trypanosoma cruzi and Host Cell. In: Nissapatorn V, Oz HS, editors. Chagas Disease - Basic Investigations and Challenges. London: InTech; 2018. doi: 10.5772/intechopen.77236.
4. Barbosa-Ferreira JM, Ortiz JV, Pessoa FG, Maria das Graças Vale Barbosa MGV, Guerra JAO, Couceiro KN, et al. Decreased Insulin Levels in Patients with Acute Chagas Disease from Brazilian Amazon treated with Benznidazole. Arq Bras Cardiol. 2025; 122(5):e20240621. doi: https://doi.org/10.36660/abc.20240621.
5. Lenzi HL, Oliveira DN, Lima MT, Gattass CR. Trypanosoma Cruzi: Paninfectivity of CL Strain during Murine Acute Infection. Exp Parasitol. 1996;84(1):16-27. doi: 10.1006/expr.1996.0086.
6. Dufurrena Q, Amjad FM, Scherer PE, Weiss LM, Nagajyothi J, Roth J, et al. Alterations in Pancreatic β Cell Function and Trypanosoma Cruzi Infection: Evidence from Human and Animal Studies. Parasitol Res. 2017;116(3):827-38. doi: 10.1007/s00436-016-5350-5.
7. Corbett CE, Scremin LH, Lombardi RA, Gama-Rodrigues JJ, Okumura M. Pancreatic Lesions in Acute Experimental Chagas' Disease. Rev Hosp Clin Fac Med Sao Paulo. 2002;57(2):63-6. doi: 10.1590/s0041-87812002000200003.
8. Santos VM, Lima MA, Cabrine-Santos M, Marquez DS, Pereira GA, Lages-Silva E, et al. Functional and Histopathological Study of the Pancreas in Hamsters (Mesocricetus Auratus) Infected and Reinfected with Trypanosoma Cruzi. Parasitol Res. 2004;94(2):125-33. doi: 10.1007/s00436-004-1183-8.
9. Saldanha JC, Santos VM, Reis MA, Cunha DF, Teixeira VPA. Morphologic and Morphometric Evaluation of Pancreatic Islets in Chronic Chagas' Disease. Rev Hosp Clin Fac Med Sao Paulo. 2001;56(5):131-8. doi: 10.1590/s0041-87812001000500001.
10. Nagajyothi F, Kuliawat R, Kusminski CM, Machado FS, Desruisseaux MS, Zhao D, et al. Alterations in Glucose Homeostasis in a Murine Model of Chagas Disease. Am J Pathol. 2013;182(3):886-94. doi: 10.1016/j.ajpath.2012.11.027.
11. Nagajyothi F, Desruisseaux MS, Weiss LM, Chua S, Albanese C, Machado FS, et al. Chagas Disease, Adipose Tissue and the Metabolic Syndrome. Mem Inst Oswaldo Cruz. 2009;104(Suppl 1):219-25. doi: 10.1590/s0074-02762009000900028.
12. Resende BAM, Beleigoli AMR, Ribeiro ALP, Duncan B, Schmidt MI, Mill JG, et al. Chagas Disease is Not Associated with Diabetes, Metabolic Syndrome, Insulin Resistance and Beta Cell Dysfunction at Baseline of Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). Parasitol Int. 2021;85:102440. doi: 10.1016/j.parint.2021.102440.